Inventory of Projects

Progress Report: Implementation of
A Public Health Action Plan To Combat Antimicrobial Resistance (Part I: Domestic Issues)
June 2003

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
Focus Area I: Surveillance			
Action Item #1: Determine Which Organisms and Susceptibility to Specific Antimicrobial Drugs Should Be under Surveillance and Create a Mechanism for Periodic Updating of This List.			
CDC, USDA, FDA, DoD, VA	Public Health Surveillance	Organisms currently under public health surveillance for antimicrobial resistance include: Campylobacter,*E. coli* O157:H7, Gram negative and Gram positive organisms causing health care associated infections, group A *Streptococcus,* group B *Streptococcus, Haemophilis influenzae, Helicobacter pylori,* HIV, Influenza, Malaria, *Mycobacterium tuberculosis, Neisseria gonorrhoeae, Neisseria meningitidis, Pneumocystis carinii,*Salmonella, Shigella, *Staphylococcus aureus, Streptococcus pneumoniae, Streptococcus pyogenes,* and *Trichomonas vaginalis.* Organisms are added to this list when resistance emerges as a public health problem, as tools are developed for detecting resistance, and when there is capacity at the appropriate level.	Ongoing.
****TOP PRIORITY**** **Action Item #2: With Partners, Design and Implement a National AR Surveillance Plan.**			

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CDC, FDA, NIH, USDA	Expand and enhance of the National Antimicrobial Resistance Monitoring System (NARMS) for enteric bacteria	NARMS is a collaboration among CDC, FDA (Center for Veterinary Medicine) and U.S. Department of Agriculture (Food Safety and Inspection Service and Agricultural Research Services). State health departments send Salmonella, Shigella, Campylobacter and *E. coli* O157:H7 isolates received at their public health laboratories to CDC for susceptibility testing. In 2001, NARMS launched the "Retail Food Study." Five participating states purchase ground beef, pork, ground turkey, and chickens from grocery stores and test them for enteric bacteria. Through NARMS, CDC provided support to the Michigan Department of Health for a program on appropriate use of antimicrobial agents in agriculture. This will foster collaboration between the state public health department and state agriculture (veterinary diagnostic) laboratories. CDC is helping develop a communit based program on appropriate use of antimicrobial drugs in animals. A model veterinary school curriculum for appropriate use will be developed, with FDA and the American Veterinary Medical Association.	Ongoing. NARMS has been expanded to all 50 states, providing national surveillance for antimicrobial resistance among foodborne pathogens. A third arm of NARMS testing retail meat samples has been added. The third testing site is FDA's Center for Veterinary Medicine's Office of Research. Foodnet sites are also submitting retail meat samples to the FDA testing site.
CDC, DoD	Gonococcal Isolate Surveillance Project (GISP)	Sentinel surveillance system for monitoring AR of *Neisseria gonorrhoeae* in the United States established in 1986. Male urethral gonococcal isolates together with clinical and demographic patient data are submitted for susceptibility testing each month from STD clinics in approximately twenty-seven cities in the United States. GISP data demonstrate the ongoing spread of fluoroquinolone-resistance and the emergence of *N. gonorrhoeae* with decreased susceptibility to azithromycin in the U.S. GISP data are published in an annual report and periodically in the MMWR.	Ongoing. GISP data were used to revise the latest version of CDC's Sexually Transmitted Diseases Treatment Guidelines which were published in 2002, and also to publish a November 2002 update on gonococcal AR in Hawaii and California in the MMWR. In 2002, several new sites were added to the sentinel surveillance system. Also in 2002, a new GISP website was launched (http://www.cdc.gov/std/gisp) which contains GISP annual reports from 1998-2001 as well as important reference and link resources. Data from 2002 will be available by Fall 2003.
CDC, FDA	Surveillance Planning	Coordinate surveillance activities.	Initial meeting was held with CDC April 2001. Interagency cooperation remains a high priority within the department. Information sharing and coordinated activities continue to increase between agencies.

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CDC	Enhanced collection and electronic transfer of data on Antimicrobial Use and Resistance (AUR)	A cooperative study of enhanced collection, compilation, and transmission of data on antimicrobial use and resistance from automated laboratory instrumentation systems in healthcare settings to CDC and other public health systems using architecture fully compatible with NEDSS. This will create a database that will facilitate benchmarking and performance feedback to promote local AR improvement efforts; development of regional, state, and national data about patterns of use and resistance; and evaluation of prevention programs.	Ongoing. During 2001, collaboration was established and funding was allocated. Specifications for reporting electronic AUR data was developed in 2002. During 2003, TheraDoc software will be modified to successfully create files with data fields in appropriate formats for downloading data in the AUR component of the National Nosocomial Infections Surveillance (NNIS) System.
CDC	Including AR surveillance in electronic laboratory-based reporting activities in the NEDSS	Develop, demonstrate, and implement automated, electronic reporting of susceptibility findings to health departments by using nationally-recognized data transmission and coding standards and sending the data through CDC's secure data network. The result of this project will enable various other AR surveillance activities to be used for this electronic communications medium.	NEDSS continues to expand its capacity to report laboratory-based susceptibility findings. During 2002, beta-testing of a NEDSS based system with unique program area modules (PAM) began.
CDC	Active Bacterial Core Surveillance (ABCs)	At 9 Emerging Infections Program sites (EIPs), surveillance is conducted for invasive bacterial diseases due to pathogens of public health importance. For each case of invasive disease in the study population, a case report with basic demographic information is filed and, in most cases, bacterial isolates from a normally sterile site from patients are sent to CDC for laboratory study. System tracks emerging AR in isolates of *Streptococcus pneumoniae* and *Neisseria meningitidis.* Data provide an infrastructure for further research, such as special studies aimed at identifying risk factors for disease, post licensure evaluation of vaccine efficacy, and monitoring effectiveness of prevention policies.	Ongoing. Program remains one of the most accurate and comprehensive surveillance tools available producing yearly summaries on emerging resistance within the 9 EIPs (California, Colorado, Connecticut, Georgia, Maryland, Minnesota, New York, Oregon, and Tennessee). A tenth site, New Mexico, was added in 2002.

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CDC	Translating lessons learned from ABCs to guide surveillance for drug-resistant*Streptococcus pneumoniae* (DRSP) in local and state health departments	A series of activities aimed at translating the lessons learned from ABCs for implementation in local and state health departments where information on DRSP is needed, but resources are limited and the goals of surveillance are more local in scope. A group of epidemiologists, microbiologists, and state health department personnel will develop a draft background document, then convene the DRSP working group to draft recommendations for surveillance at state and local health departments. This meeting would include representatives from sites planning to do local or state surveillance, as well as national, state, and local public health representatives and DRSP authorities.	Ongoing. This program includes CDC, state epidemiologists and laboratory personnel interested in conducting surveillance for DRSP. A roundtable was held at CSTE's Annual Conference in June 2002. The DRSP/MRSA Surveillance Conference was held in March 2003, and state consultations have been provided. Representatives from ov 40 states and territories attended the DRSP/MRSA surveillance conference in March 2003. The DRSP surveillance manual should be completed in July 2003.
CDC	National Healthcare Safety Network (NHSN)	The NHSN will be an Internet-based nationwide network that will monitor trends in adverse events associated with invasive devices, procedures, and medications used in the delivery of healthcare. Under the NHSN's Medication-associated Adverse Event Module, initial focus will be on use and resistance of antimicrobial agents and on establishing electronic reporting of antimicrobial use and resistance data to increase efficiency, timeliness, and accuracy of the monitoring effort. When implemented, the NHSN will significantly enhance the ability to monitor and track trends of usage and resistance of microbes to antimicrobial agents in a variety of healthcare delivery settings. These data can then be used to enhance patient safety by enabling healthcare workers to develop and deploy strategies to prevent overuse and inappropriate use of these agents, as well as strategies to prevent other pathogens from becoming resistant.	Initiated. In 2001-2003, gathered requirements for system, held joint application development sessions with current and potential users, and started work on data model, security, standard nomenclature for pathogens and antimicrobial agents, and detailed use cases that define system functionality. In addition, work has been ongoing to develop the messaging specifications for electronic reporting from hospitals of antimicrobial use (from pharmacy systems) and resistance (from microbiology systems). Also in 2003, began work to design, develop, and deploy the NHSN (beta-testing scheduled for Fall 2003 with deployment of version 1.0 in January 2004).
CDC	The National Nosocomial Infections Surveillance (NNIS) System.	A cooperative effort between the CDC and >300 hospitals to create a national nosocomial infections database. The database is used to reveal the epidemiology of nosocomial infections and to show AR trends, among other purposes.	Ongoing. The data from the NNIS System are reported annually in the NNIS Report which appears on the NNIS Web page (http://www.cdc.gov/ncidod/hip/SURVEILL/NNIS.HTM) and in the December issue of the*American Journal of Infection Control*.

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CDC	Surveillance projects of HIV antiretroviral drug resistance	Surveillance for HIV antiretroviral drug resistance among different populations (adult, adolescent, and pediatric) and geographic areas in the U.S. using different methodologies, focusing on genotypic testing but also including phenotypic testing. Determine transmission of drug-resistant strains to previously uninfected persons and from mother to infant. Results support experts in deliberating potential recommendations for antiretroviral resistance testing before treating drug-naïve new patients. Results also provide information to guide regimens for post-exposure prophylaxis and prevention of mother to child transmission during pregnancy and delivery transmission. Could contribute to evaluation of success of risk prevention measures directed towards HIV-seropositive patients in treatment.	Ongoing. Funds awarded to participating state and local health departments. Laboratory characterization of transmitted HIV identified in drug-naïve persons was continued and data analyzed. The data highlighted the clinical implications of various key mutations. Novel methods for rapid phenotypic detection of drug resistance were published:1) Garci-Lerman et al. (2002) Antimicrobial Chemotheraphy, 50:771-774.2) Qari et al. (2002) Antiviral Therapy, 7:131-139. In 2003, beginning antiretroviral resistance testing among newly diagnosed persons with HIV in 26 states and the Pilot Antiretroviral Drug Resistance Testing (ARVDRT) Project in four states.
CDC	National Tuberculosis Surveillance System (NTSS)	Ongoing collection, analysis, and communication of national tuberculosis surveillance information; expanded in 1993 to include the frequency and type of AR, enabling strategically focused tuberculosis control and elimination efforts. The expanded national TB surveillance system has proven its usefulness in assisting in the evaluation of the success of TB control efforts and monitoring the status of the epidemic, particularly through the collection of data on initial drug susceptibility. Information on the use of initial regimens of four first-line drugs, directly observed therapy, and completio of therapy in one year or less have been used as measures to evaluate program success. As future efforts towards TB elimination increase, both existing and new surveillance systems at the national, state, and local levels will become even more critical to monitor the burden and impact of TB, evaluate the success of control and prevention efforts, and direct planning and policy development.	Ongoing. Data collection and analysis are gathered on a continuous basis. Since 1993, the proportion of patients with multidrug-resistant (MDR) TB in the United States has decreased, from 3% to 1% in 2001. Of the total number of reported MDR TB cases, the proportion occurring in foreign-born persons increased from 31% (150 of 482) in 1993 to 73% (101 of 138) in 2001. Tables 8, 9, and 32 of the CDC annual TB surveillance report, Reported Tuberculosis in the United States, 2001, provide detailed summaries of anti-TB drug resistance from the national surveillance data. This report and other publications and recommendations based o these data are available on the internet (http://www.cdc.gov/nchstp/tb/pubs/pem.htm).

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CDC	Estimate of the burden of MRSA disease in hospitalized adults	This project uses existing datasets to measure the annual incidence of MRSA disease in hospitalized adults.	In 1999-2000, there were 292,687 hospitalizations with diagnosis of *S. aureus* infection estimated annually, accounting for 0.8% of hospital discharges. The average methicillin resistance rate was 42.0%. 119,760 hospitalizations with diagnosis of MRSA infection were estimated annually, including 30,015 septicemias, 26,726 pneumonias, and 63,019 other infections, accounting for 0.3% of hospital discharges. Estimates in non-hospitalized persons are planned for 2003.
CDC	The epidemiology of MRSA strains in the U.S., using PulseNet	PulseNet is an innovative, laboratory-based national surveillance program that tracks the pulse-field gel electrophoresis (PFGE) profiles of selected bacteria. In collaboration with state health departments, MRSA strain types and their AR profiles in the U.S. are monitored through PulseNet to determine similarity with MRSA strains throughout the country, the prevalence of MRSA strain types from which vancomycin-intermediate strains of MRSA are derived, and similarity of U.S. epidemic strains of MRSA to those known to cause outbreaks and epidemics in Europe, Canada, and the Far East.	Ongoing. Data from this nationwide system have already been used to begin to understand the spread of specific MRSA strains among certain groups of patients in hospitals and in the community and will provide a clearer picture of the pathogenicity of *S. aureus* and the spread of AR among staphylococci. Recent PFGE data have been extremely useful for monitoring the spread of MRSA isolates in the United States. PFGE data have indicated the presence of seven major clonal lineages or pulse-field types (PFTs) of MRSA in the U.S. Four PFTs are common among healthcare related strains, two PFTs are found primarily among community-acquired isolates, and one is found amor strains from both healthcare and community-acquired strains.

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CDC	Surveillance for Emerging Antimicrobial Resistance Connected to Healthcare (SEARCH)	Normally, vancomycin is the most reliable and effective drug for treating MRSA. The appearance of MRSA with reduced susceptibility [to vancomycin] (vancomycin-intermediate *Staphylococcus aureus* [VISA]), and resistance (vancomycin resistant *Staphylococcus aureus* [VRSA]) is concerning and may be a warning that strains resistant to vancomycin could soon appear. SEARCH is a network of voluntary participant (i.e., hospitals, private industries, professional organizations, and state health departments) which have joined together to report the isolation of*Staphylococcus aureus* with reduced susceptibility to vancomycin. All U.S. healthcare organizations or practitioners are encouraged to report such isolates to SEARCH and, after notifying their state health department, to send the isolates to CDC for confirmatory testing. SEARCH enhances the ability to detect these pathogens, which have a high public health importance but are difficult to detect through traditional surveillance systems, and provides confirmatory diagnostic and expedited susceptibility testing for these isolates when local testing is n	Ongoing. In 2001, laboratories participating in SEARCH processed over 300,000*Staphylococcus aureus* isolates. Of these, twenty-four strains were sent to CDC for expedited vancomycin susceptibility testing. CDC confirmed one VISA and seven strains with reduced susceptibility to vancomycin or near-VISAs (vancomycin MIC=4 µg/ml). To date, CDC ha identified eight VISAs and two VRSAs in the U.S. Updated guidance on appropriate testing was sent to State Health Departments in April, 2003.
CDC	MRSA carriage in rural Alaska	In recent years, several community outbreaks of MRSA skin infections have occurred among Alaska Natives. This is a survey of the frequency of MRSA nasal colonization in twelve rural Alaska communities. The findings will be disseminated to affected communities and health care providers to help promote appropriate antimicrobial drug use and promote prevention of MRSA skin infections.	Ongoing.

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CDC	Antimicrobial resistant early-onset sepsis and maternal intrapartum antibiotic use	Increased use of antibiotic prophylaxis during labor and delivery to prevent perinatal group B streptococcal (GBS) disease has decreased the rate of early-onset GBS infections by 70%. As more antimicrobial drugs are used in the labor and delivery setting directed at prevent mother-to-child transmission of group B streptococcus, the risk that among newborns exposed to other perinatal pathogens, such as *E. coli* drug resistant infections might increase. The objectives of this project were to determine the rate of early-onset infections with drug resistant *E. coli* in selected areas, to evaluate whether antimicrobial drug use during labor and delivery was associated with an increased risk of drug resistant *E. coli*, and to assess the impact of a penicillin G shortage on prophylactic use of penicillin, ampicillin, and other agents during labor and delivery.	Surveillance for resistant *E. coli* sepsis in the first week of life is ongoing in the Active Bacterial Core Surveillance (ABCs) with a new surveillance area, MN, starting case finding in 2003. To date surveillance has led to two publications summarizing data from CT , GA, and CA. Although the overall rate of ampicillin resistant *E. coli* remained stable from 1998-2000, the rate of resistant *E. coli* infections increased among preterm infants, particularly among very low birthweight infants. Although very low birth weight infants make up a small proportion of overall births, this raises some concern and surveillance will be ongoing, with plans to look trends in 2001 and 2002, a more detailed look at the association between intrapartum antibiotic exposure and risk of resistance, and the impact of new recommendations for intrapartum vancomycin prophylaxis of penicillin allergic women to prevent perinatal group B streptococcal disease.
CDC	Vancomycin-tolerant and vancomycin-resistant *Streptococcus pneumoniae*: developing a preparedness plan and enhancing surveillance	Recently, clinical isolates of *S. pneumoniae* that can survive, but not reproduce, in the presence of vancomycin (vancomycin-tolerant strains) were identified. Investigations of the biological mechanism of vancomycin tolerance suggest that tolerance may also be a precursor to vancomycin resistance. This project will evaluate the reproducibility of vancomycin-tolerance testing, determine the prevalence of vancomycin tolerance among pneumococcal meningitis patients in the U.S., and evaluate the clinical implications and identify risk factors for meningitis caused by vancomycin-tolerant pneumococci. In addition, CDC will develop a preparedness plan for the investigation and control of vancomycin-resistant pneumococci, should it emerge.	Ongoing. Current efforts focus on attempting to verify that vancomycin tolerance testing can be duplicated in multiple laboratories. A draft preparedness plan for the emergence of vancomycin resistant pneumococci has been developed and was updated in 2002 based on lessons learned from vancomycin-resistant *Staphylococcus aureus*. All surveillance isolates from 2001 and 2002 were tested for susceptibility to vancomycin and were found sensitive.

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CDC	The *Helicobacter pylori* Antibiotic Resistance Program (HARP) and Antimicrobial resistance in *Helicobacter pylori* in Alaska	HARP conducts prospective, long-term monitoring of trends in AR to guide treatment regimens for *H. pylori* infections. Twelve academic medical centers throughout the United States submit *H. pylori* isolates and clinical and epidemiologic data from endoscopically-diagnosed patients monthly. Resistance is tested at CDC. Resistance and epidemiologic data are entered into a database at CDC for analysis of prevalence, risk factors and regional trends in rates of antimicrobial resistance in *H. pylori* strains. The monitoring laboratory is also used for ongoing collaborative CDC-Emory-Veterans' Administration Medical Center research of *H. pylori* and peptic ulcer disease, and is a future platform for collaborative studies between academia, public agencies, and industry. A sentinel surveillance system for *H. pylori* has been established in Alaska to monitor antimicrobial resistance among Alaska Natives who have high rates of *H. pylori* infection; and where AR among *H. pylori* is high.	Ongoing. Manuscript reporting incidence and risk factors for AR over the first four years of the study will be submitted to journal in June 2003. In 2001, susceptibility testing methods established by FDA and National Committee on Clinical Laboratory Studies (NCCLS) for antimicrobial susceptibility testing of *H. pylori* were validated, and the minimum inhibitory concentration with quality control limits for antimicrobial agents such as amoxicillin, clarithromycin, metronidazole, and tetracycline were determined. Analysis of data from HARP show that nearly 40% of isolates are resistant to one or more first-line antimicrobial agents. These findings may form the basis of recommendations for treatment. Completion of the native arm of *H. pylori* study in Alask was completed and recruitment of non-native arm is in progress. Results expected soon.
CDC	Molecular tools for the control and epidemiology of head and body lice	Evaluate new molecular tools for monitoring louse populations and determining the role of insecticide resistance in louse infestations and re-infestations to design and implement appropriate control strategies. Characterize local populations of lice and the global relationships and movements of louse populations. Ascertain the genetic relationships of head, body, and pubic lice. When completed, the data generated will improve knowledge of the epidemiology of insecticide resistance in louse populations and improve prevention and control strategies.	Ongoing. In 2001, collected head and body lice from over te states and seven countries, and sequenced over 700 clones from gene libraries. In 2002, the microsatellite markers developed through our sequencing of head and body louse libraries were applied in field studies of head and body louse population biology and micro-epidemiology of insecticide resistance. These studies are providing the data needed to assess the interaction of multiple resistance alleles and louse micro-epidemiology around the world, and will result in rapid increase in our understanding of louse resistance and micro-epidemiology.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CDC	Testing of drug-resistant *Trichomonas vaginalis*	Trichomoniasis is the most common curable STD in young, sexually active women. This project includes passive surveillance for *Trichomonas vaginalis* resistance among isolates from patients whose infection has not resolved after at least two courses of standard metronidazole therapy. Parasites are tested both aerobically and anaerobically for sensitivity to metronidazole and to tinidazole, which, outside the United States, is the most common alternative therapy for trichomoniasis. These data will identify molecular markers of metronidazole-resistant strains, allow investigation of drug-resistance mechanisms, and will be utilized to identify alternative chemotherapeutic agents.	Ongoing. Testing is an ongoing service of CDC. In 2001, initiated testing on isolates obtained through the Grady Adolescent STD Project (GRASP) to determine the prevalence of metronidazole-resistant *T. vaginalis* isolates in an urban adolescent clinic. Isolate testing and data analysis is an ongoing process and results will prove useful in identifying alternate therapies.
CDC	Enhanced surveillance of influenza viruses for resistance to licensed drugs and development of tests for rapid detection of drug-resistant strains with pandemic potential	Improved molecular tests for rapid diagnosis of mutants resistant to both the old and new drugs are needed for pandemic preparedness as well as for interpandemic control of influenza. This project studies avian influenza viruses of different subtypes, which will improve pandemic preparedness. In addition, it will evaluate existing biochemical tests and develop new molecular techniques for detecting influenza A and B mutants resistant to neuraminidase inhibitors (NIs), which will improve surveillance for drug-resistant variants among human influenza viruses.	In 2001, compared assays for resistance of influenza viruses to NIs to determine the most adequate method for further use in detecting of NI-resistant strains, and analyzed sequencing data available for avian influenza viruses with the goal of developing molecular techniques for rapid diagnosis of adamantane (amantadine or rimantadine)-resistant mutations among avian influenza viruses of different subtypes was initiated. In 2002, two neuraminidase (NA) assays, fluorescence (FL) and chemiluminescent (CL), were applied to routinely monitor more than a thousand influenza field isolates collected worldwide during the 2000-2002 seasons for susceptibility to licensed NIs.
DoD	Development of a DoD AR surveillance plan consistent with the national AR surveillance plan	Establish an overarching framework for facilitating the implementation, operation, and evaluation of activities in AR surveillance within DoD.	Leaders in infectious disease, laboratory, and preventive medicine in the three services are working to develop a common plan for AR surveillance in the DoD.

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DoD	DoD AR surveillance network	Under a Cooperative Research and Development Agreement (CRADA) with private industry, developing a DoD-wide AR surveillance network for identifying AR occurrences and trends within the military population. The cornerstones of thi mechanism are: 1) the provision of daily, independent quality assurance review and feedback of a military laboratory's susceptibility test results by experts in the field, 2) the continuous generation of up-to-date antibiograms based on an individual medical facility's AR patterns, 3) access to validated information on antimicrobial resistance occurrences and trends in the facility's geographic region for evaluating their implications for military personnel, and 4) facilitation of DoD-wide monitoring of AR trends to improve evidence-based decision and policy making on antibiotic usage and patient care, and 5) to enhance DoD ability to identify and respond to AR events of military significance in a timely manner.	Electronic antimicrobial susceptibility testing quality assurance and analysis system installed in three pilot sites completed. Linkage of sites into a DoD network for information sharing and analysis of AR trends completed. Expansion of network and its evaluation planned.
VA	Emerging Pathogens Initiative (EPI)	The Veterans Health Administration (VHA) currently has an ongoing and well-defined AR surveillance plan (the EPI, a laboratory-based automated surveillance system).	Currently over 170 VHA facilities across the country transmit data to the EPI monthly. The data collected by the EPI are reviewed quarterly by the Infectious Diseases Program Offic and reported to the Veterans Integrated Service Networks. There is an updated version in final stages for implementatic that includes antibiotic resistant organisms.
VA	Emerging Pathogens Initiative (EPI)	The VHA uses standardized definitions and methods to set local parameters for surveillance in the EPI system. Current EPI data regarding some AR organisms are returned to the Veterans Integrated Service Networks quarterly with reporting station specific data included. National quartiles are also provided for use at the Network and local level. Confidentiality is a key element in any activity undertaken by the VHA. Great effort has been put forth to maintain confidentiality of the Emerging Pathogens Initiative surveillance data set. Access is strictly limited for any data with unique identifiers.	Ongoing.
FDA	Proposed Rule – Surveillance/Reporting	Publish proposed rule regarding surveillance and annual reporting (included with proposed rule "Safety Reporting for Human Drug and Biologic Products").	Assessing economic impact of the proposed regulation.
FDA	Guidance - Surveillance Planning	Develop guidance relating to surveillance and annual reporting (based upon proposed rule "Safety Reporting for Human Drug and Biologic Products").	Assessing economic impact of the proposed regulation.

Action Item #3: Develop Standards and Methodologies.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CDC	A surveillance system for tracking and characterizing drug treatment failures in*Pneumocystis carinii* pneumonia	Because of the widespread use of trimethoprim-sulfamethoxazole and atovaquone for treatment and prophylaxis of PCP, AR monitoring is of great importance. Because direct sensitivity testing is currently not possible wit human *P. carinii*, work in this area has focused on molecular methods that look directly for mutations in the genes that encode the specific enzymes that are targeted by anti-*Pneumocystis* drugs. This project will study specific mutations at genetic positions that determine key drug enzyme-binding sites in an effort to correlate these mutations with treatment and prophylaxis failure data that are collected through patient questionnaires and chart abstractions. The results of this study will indicate where resistance appears to be in the process of emerging and whether continued or mor widespread surveillance is indicated.	Specific mutations at genetic positions that determine key drug enzyme binding sites were studied in an effort to correlate these mutations with treatment and prophylaxis failure data that were collected through patient questionnaire and chart abstractions. Analysis completed for specimens and data collected to date.
CDC	Grant Program: Applied Research on AR - Validation of National Committee for Clinical Laboratory Standards (NCCLS) Breakpoints for Bacterial Human Pathogens	The purpose of the program is to provide assistance for applied research aimed at prevention and control of the emergence and spread of AR in the United States. This program will focus on validation of NCCLS breakpoints for bacterial human pathogens of public health importance. This research includes three components that will provide information needed to prevent and control AR: (1) validating existing interpretive criteria for pathogens of public health importance; (2) developing new interpretive criteria for pathogens of public health importance using existing NCCLS methods and quality control; and (3) developing new interpretive criteria and new antimicrobial susceptibility testin methods for pathogens of public health importance using existing NCCLS methods and quality control as a starting point for novel test development.	Funded three programs in the Fall of 2002: University of Texas Medical Center, (Development of Interpretive Breakpoint Criteria for Neisseria Meningitidis); University of Pittsburgh, (NCCLS Interpretive Criteria for Salmonella); University of Wisconsin Medical Center, (Validation of NCCLS Methods and Breakpoints for Extended Spectrum beta-lactamases).
Action Item #4: Address Additional Surveillance Issues Unique to AR.			

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CDC	Specialized surveillance projects and treatment trials for drug-resistant tuberculosis	Information on the initial drug regimen prescribed, coupled with information on initial drug susceptibility results, allows a judgment about the adequacy of therapy and corrective actio on individual cases of tuberculosis by public health officials and health care providers, if the regimen is judged to be inadequate or suboptimal. To improve knowledge of drug resistance in tuberculosis and effectiveness of alternate treatment regiments, CDC is conducting projects on the frequency of low-level INH resistance and resistant to quinolones, treatment of HIV-related tuberculosis using a rifabutin-based regimen, and a trial to determine the effectiveness of a new regimen for isoniazid-resistant tuberculosis. Results of these studies will describe prevalence and incidence of understudied resistance in tuberculosis and inform recommendations for new treatment regimens.	Ongoing.
CDC	See Action Item #5 (monitoring antimicrobial use in community and correlating usage with resistance patterns).	See Action Item #5 (Monitoring antimicrobial use in community and correlating usage with resistance patterns).	See Action Item #5 (Monitoring antimicrobial use in community and correlating usage with resistance patterns).
FDA	Antimicrobial surveillance plan	Development of a surveillance plan for antimicrobial drug resistance among clinical laboratory isolates.	A five year option contract was awarded to Focus Technologies in October 2002.
FDA	See Action Item #2 (Proposed Rule - Surveillance/Reporting).	See Action Item #2 (Proposed Rule Surveillance/Reporting).	See Action Item #2 (Proposed Rule -Surveillance/Reporting).
FDA	See Action Item #2 (Guidance).	See Action Item #2 (Guidance).	See Action Item #2 (Guidance).

**** TOP PRIORITY ****

Action Item #5: Develop and Implement Procedures for Monitoring Antimicrobial Use In Human Medicine, Agriculture, Veterinary Medicine, and Consumer Products.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CDC	AUR: component of the National Nosocomial Infections Surveillance (NNIS)	The AUR component of NNIS allows participating hospitals t collect data on select antimicrobial agents and cumulative susceptibility data on select organisms identified by the clinical microbiology laboratories, allowing the calculation of a national estimate of the prevalence of antimicrobial-resistant organisms in hospitals and the amounts of select antimicrobial agents used in these hospitals. These data allow select AR rates to be compared among hospitals and provide better understanding of the relative importance of antimicrobial drug use vs. other factors (i.e., cross-transmission, severity of illness) for development of antimicrobial-resistant infections by several key pathogens	Ongoing. In 2001, implemented the AUR component and received data from fifteen hospitals. 2002 saw an increase in hospitals responding to twenty and development of a pilot system to electronically capture susceptibility testing results to simplify reporting.
CDC	Monitoring antimicrobial use in the community and correlating usage with resistance patterns	Analysis of antimicrobial use databases has proven to be complex, requiring sophisticated statistical methods to adjust for the design of certain usage survey samples and requiring substantial medical consultation time to link drug use with appropriate clinical diagnosis codes and potentially with databases regarding resistant infections. This project will develop a core analytic team that will track antimicrobial drug use in the community and correlate results of use with drug-resistance patterns (using drug-resistant*Streptococcus pneumoniae* as the marker community-acquired respiratory organism) and with community intervention efforts. The team will review availability and appropriateness of antimicrobial use databases and focus on establishing baseline trends in prescribing for upper respiratory infections using NAMCS, National Hospital Ambulatroy Medical Care Survey (NHAMCS), state Medicaid databases, Synergy, and other databases provided through partners (e.g., Blue Cross/Blue Shield; specific managed care organizations).	Ongoing. In 2001, analyzed and published trends in prescribing for respiratory conditions in the community during the 1990s by using NAMCS and NHAMCS, initiated development of standard programs and documentation for regular analyses of three national or regional databases for drug prescribing, and provided technical support to five intervention programs or partners. During 2002, completed and published analysis of national data on trends in antibiotic prescribing for children for upper respiratory infections (McCaig et al. JAMA June 2002), issued new recommendations for alternative antibiotics for group B streptococcal prophylaxis for penicillin allergic women .
CDC	National Ambulatory Medical Care Survey (NAMCS)	An annual national survey that collects data on the utilization of ambulatory medical care services provided by office-based physicians in the united States. Findings are based on a sample of visits to nonfederally employed office-based physicians who are primarily engaged in direct patient care. NAMCS monitors trends in prescription of antimicrobial drugs in the physician office setting.	Ongoing. Recent NAMCS methodology, data, and reports are available on the internet: (http://www.cdc.gov/nchs/about/major/ahcd/ahcd1.htm

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CDC	Comprehensive demonstration project: building regional coalitions to prevent methicillin-resistant *Staphylococcus aureus* in healthcare facilities	This project supports the development and implementation of comprehensive programs to reduce the incidence of MRSA infections in states and/or large regional networks acute phase and nonacute phase healthcare facilities. The Pittsburgh Regional Healthcare Initiative (PRHI) was recruited as a collaborating partner for this project. PRHI is a coalition of regional healthcare facilities and civic, corporate, and healthcare leaders in the Pittsburgh area dedicated to improving the quality of healthcare delivery in southwestern Pennsylvania. An intervention plan is being developed which involves applying a process engineering technique borrowed from the automotive industry Toyota Production System (TPS) to the processes of patient care that contribute to the problem of AR. The technique is designed to maximize the quality and efficiency of complex systems of work. Improving the design and flow of work should remove barriers to compliance with recommended prevention strategies.	Ongoing. Initiated pilot testing of the interventions in two hospitals within the network (University of Pittsburgh Medical Center-Presbyterian Hospital and Pittsburgh Veterans Administration Hospital) during 2001. Baseline compliance with infection control practices such as hand hygiene was lo (e.g., 19% hand hygiene compliance on entry for MRSA patient encounters). Follow-up observations show significant improvement in compliance across all occupations. Problems hindering compliance which continue to be targete include unreliable delivery of isolation materials, inconsisten identification of patients requiring isolation, and time consuming inefficiencies in the delivery of patient care services such as medication administration. In addition, an assessment of policy, perception, and practice regarding MRSA control has been initiated.
DoD	Prescription databases	In 2001, DoD developed a prescription database as part of a patient safety program. This database is used principally to screen for drug-drug interactions resulting from patients filling their prescriptions in more than one medical treatment venue Its linkage to a DoD syndromic surveillance system (ESSENCE) is being attempted. Once this is achieved, and when the AR surveillance system is more mature, a further link is planned to permit trends in detected AR to be analyzed with respect to prescription practices and patient presentations.	Initiated prescription database. Linkages continue to be developed.
VA	Emerging Pathogens Initiative (EPI)	Resistance data are being gathered in the EPI, an automated surveillance system, at the reporting site level and can be used for comparisons based on geographic areas and can be linked to ICD-9-CM diagnostic codes. In addition, drug use data can be linked to laboratory testing and diagnoses, particularly as it relates to hepatitis C, a significant emerging disease.	This item is already underway in the VHA with reporting from facilities across the country. There is an updated version in final stages for implementation that includes antibiotic resistant organisms.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
FDA	See Action Item #4 (Antimicrobial surveillance plan)	Review private sector surveillance data to determine whether it has potential to support FDA/CDER regulatory and scientific activity.	See Action Item #4 (Antimicrobial surveillance plan)
FDA	See Action Item #2 (Proposed Rule Surveillance/Reporting).	See Action Item #2 (Proposed Rule Surveillance/Reporting).	See Action Item #2 (Proposed Rule Surveillance/Reporting).
FDA	See Action Item #2 (Guidance).	See Action Item #2 (Guidance).	See Action Item #2 (Guidance).
Action Item #6: Identify and Evaluate Methods for Collecting (e.g., Optimal Sampling Methods) and Disseminating the Surveillance Data on Antimicrobial Drug Use.			
FDA	See Action Item #4 (Antimicrobial surveillance plan)	See Action Item #4 (Antimicrobial surveillance plan)	See Action Item #4 (Antimicrobial surveillance plan)
FDA	See Action Item #2 (Proposed Rule Surveillance/Reporting).	See Action Item #2 (Proposed Rule Reporting/Reporting).	See Action Item #2 (Proposed Rule Reporting/Reporting).
FDA	See Action Item #2 (Guidance).	See Action Item #2 (Guidance).	See Action Item #2 (Guidance).
Action Item #7: Work With Accrediting Agencies To Address Antimicrobial Drug-Use As Part Of Quality Assurance In Health Care Delivery Systems.			
Action Item #8: Ensure That Clinical Laboratories That Provide Data for AR Surveillance Purposes Have Access to and Routinely Participate in Pertinent Training and Proficiency Testing Programs with Good Performance and Indicate AR Testing Methodologies in Their Surveillance Reports (e.g., Specific Automated Methods or Manual Techniques).			
CDC	Lab Errors: CD-ROM for susceptibility testing	New antimicrobial agents and new resistance patterns pose a challenge to clinical laboratories methods of testing because testing methods vary with organism/antimicrobial agent combinations. NCCLS standards outline recommended procedures, but are difficult for some laboratories to interpret. This CD assists laboratories in applying NCCLS standards, demonstrates the modes of action of each group of antimicrobial agents and the mechanisms organisms develop to resist the agents, describes quality control procedures needed to verify accuracy of testing results, and demonstrates specific procedures laboratories must use to detect resistance in different organisms. Available at from: http://www.aphl.org/ast.cfm	CD-ROM was completed in 2002 and has been distributed widely throughout the US and across the world.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CDC	Multilevel Antimicrobial Susceptibility Testing Educational Resource (M.A.S.T.E.R.) Program	The M.A.S.T.E.R. program, is a 3-phase project to upgrade the accuracy of antimicrobial susceptibility testing and reporting in the U.S. Currently, the Web site has case studies, a Q and A section, hot papers, and a list of references. http://www.phppo.cdc.gov/dls/master/aboutmaster.asp	Project ongoing. The website received over 130,000 hits from 30 countries. Material from the website was used in numerous training courses on susceptibility testing and is frequently cited as a resource in medical technology classes.
CDC	Reducing laboratory errors associated with detecting and reporting antimicrobial-resistant bacteria from blood cultures (Iowa)	The goal of the Iowa project is to assess the accuracy of the bacterial identification and antimicrobial susceptibility testing data appearing in patients' charts in 15 hospitals for organisms isolated from positive blood cultures. Blood culture isolates are sent to CDC for confirmation of identification and susceptibility testing. These results are compared to the results from the original laboratory report and the results retrieved from the patients' charts. The accuracy of the reports and the appropriateness of the antimicrobial agent reported are assessed. This project should provide important feedback information regarding inappropriate reporting of test results to the patients' charts and thus improve laboratory accuracy. By reporting only necessary AR results to the patients' charts, we should, in turn, improve antimicrobial prescribing in the hospitals in the study.	During 2001, blood culture isolates were collected from sixteen different hospitals in Iowa, identifications and susceptibility test results were completed at CDC, and the results were collated and reviewed with other data in Iowa. During 2002, data analysis was completed and a study to determine the effectiveness of educational materials on testing and reporting of laboratory results was conducted. Manuscript on project is in progress.
CDC	AR research and reference testing	CDC reference laboratory conducts ongoing research and provides selected reference services for susceptibility testing of numerous bacterial species.	Ongoing. Recent achievements include the description of new AR mechanisms, which has led to modification and improvement of the testing methods used in clinical microbiology laboratories to detect resistance, evaluations of NCCLS methods completed and modifications made to improve accuracy, and evaluations of commercial susceptibility testing methods completed and problems noted to the manufacturers. Additional accomplishments include confirmation and investigation of phenotype and genotype of the first two vancomycin-resistant *Staphylococcus aureus* isolates in the United States.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CDC	*Mycobacterium tuberculosis* (Mtb) antimicrobial susceptibility testing program	Approximately 160 laboratories participate in this program designed to assess and enhance the ability of clinical laboratories to accurately test for AR. Most laboratories test for susceptibility to isoniazid, pyrazinamide, ethambutol and rifampicin, and streptomycin. Approximately 35 laboratories test nontuberculous mycobacteria in addition to susceptibility to other drugs. Laboratories can view reports of results on a website address for each panel shipment for feedback.	Ongoing.
Action Item #9: Evaluate the Performance of Licensed, Automated AR Testing Devices in the Context of Changing Resistance Patterns and Update Their Labeling When Appropriate (e.g., Changes in Quantitative Resistance That May Make a Test Result Invalid).			
Action Item #10: Working with Partners, Including National Committee for Clinical Laboratory Standards (NCCLS), Further Develop, Refine, and Promote Standardized Clinical, Epidemiologic, and Laboratory Methods for Documenting and Assessing the Significance of Drug Resistance Among Yeasts and Moulds, Parasites, and Viruses.			
FDA	In-vitro antimicrobial susceptibility testing	Develop quality control standards for the in-vitro antimicrobial susceptibility testing of bacterial pathogens isolated from aquaculture foods.	Initiated studies 2001.
FDA	Devices containing antimicrobials guidance	Draft guidance document for industry: how the Center for Devices and Radiologic Health (CDRH) intends to regulate devices containing antimicrobial agents, and what information regarding efficacy and resistance CDRH wants to see in	In development.
FDA	HIV Drug Resistance Genotype Assay Guidance	Revised guidance on HIV Drug Resistance Genotype Assays. Significantly reduces the extent of studies required for clearance.	Publication pending.
Action Item #11: Identify Ways To Overcome Economic, Legal, and Other Barriers To Appropriate AR Testing and to the Reporting of Results (e.g. Sufficient Human Resources, Cost Considerations, Empiric Treatment Recommendations, Managed-Care Practices, etc.).			

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CDC	Economic modeling of diagnostic and treatment strategies for gonorrhea based on prevalence of AR	The increasingly widespread use of nonculture methods for gonorrhea diagnosis is a major challenge to monitoring AR in *N. gonorrhoeae*, especially in light of the emergence of ciprofloxacin-resistant gonococcal isolates from Hawaii (ciprofloxacin is first-line gonorrhea therapy). This project will examine which diagnostic and treatment strategies are more cost-effective when the proportion of *N.gonorrhoeae* that are ciprofloxacin-resistant is less than 5%: continue to use ciprofloxacin and implement more widespread susceptibility testing, or switch to a more expensive cephalosporin and not increase the scope of susceptibility testing. When completed, the results will help provide a rational basis for programmatic decisions both for selection of gonorrhea treatment and for use of laboratory resources.	Ongoing. Manuscript in progress.
Action Item #12: Pursue Legal Mechanisms for Manufacturers To Provide Otherwise Unavailable Drugs to Government Reference Laboratories for the Sole Purpose Of Antimicrobial Drug Susceptibility Testing (as part of surveillance) with the Understanding That These Drugs Will Not Be Used for Drug Discovery Purposes.			
Action Item #13: With State Health and Agriculture Departments and Other Stakeholders, Define Needed Core Capacity (Human, Laboratory, and Electronic Resources) at the State and Local Level To Ensure That Basic AR Surveillance Is Conducted In These Jurisdictions. As Part of This Effort, Ensure That State Public Health and Veterinary Diagnostic Laboratories Maintain the Capacity To Test the Drug-Susceptibility Patterns of Resistant Organisms of Public Health Importance, Especially For Drug-Microorganism Combinations for Which Testing Mechanisms Are Not Routinely Available at Hospital and Commercial Laboratories.			
Action Item #14: Provide Resources To Assist In Meeting State and Local Core Capacity Needs for AR Surveillance. Strive To Provide Consistent Funding from Year to Year to State and Local Health and Veterinary Diagnostic Laboratories That Meet Quality Assurance Standards.			
Action Item #15: Provide an Accessible, Centralized Source of AR Data from Major Surveillance Systems Involving Animal and Human Populations. In Consultation with Stakeholders, Determine How To Report AR Data in a Way That Is Valid and Useful to Interested Parties (e.g., Clinicians, Public Health Officials, Veterinarians, and Researchers). Include Sufficient Detail in Surveillance Reports To Permit Local Analysis and Comparison with Trends in Drug Use and Medical and Agricultural Practices.			

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
DoD	Surveillance for *Streptococcus pyogenes* among military trainees	Increasing resistance to macrolide antibiotics has been demonstrated for *S. pyogenes* isolates. Furthermore, during military-recruit training exercises, penicillin-allergic patients are often given erythromycin when mass prophylaxis is recommended. If resistant organisms are present or develo in this population, *S. pyogenes* infections (latent or overt) may not be treated effectively. Recruits could become reservoirs of resistant pathogens for military populations. This project conducts antimicrobial susceptibility and gene typing on *S. pyogenes* isolates collected from recruits at military training centers and monitors for *S. pyogenes* resistance rates. As of September 2002, the resistance rates detected in the recruit population were the following: erythromycin (5.3%), clindamycin (2.5%), tetracycline (4.6%), and 0% for penicillin, levofloxacin and vancomycin. Temporal trends in antibiotic resistance among *S. pyogenes* isolates demonstrated no discernible patterns.	Reports of susceptibility test results and summary statements are being provided to the primary care facility, are accessible to DoD staff on the website www.geis.ha.osd.mil and have been used in presentations at national meetings. Generated data show moderate AR rates as of 2002.
DoD	Surveillance of antibiotic-resistant *S. pneumoniae* in military populations	Antibiotic resistance in *S. pneumoniae* has risen dramatically over the last decade, with varying levels of resistance found different regions of the country. Similarly, *S. pneumoniae* causes significant morbidity among populations served by U.S. military medical centers. In this study, *S. pneumoniae* isolates from selected U.S. military medical centers are being serotyped, subtyped, and tested for antibiotic resistance. As of September 2002, full or partial penicillin resistance was found in 35% of the isolates, with 23% having resistance to three or more antibiotics. This represents no discernable change in rates from 2001.	Reports of resistance findings and trends are being shared with the contributing medical centers, and summary statements are available through the website http://www.geis.ha.osd.mil Study findings have been presented at national meetings and in peer-reviewed publications.
DoD	Surveillance of *Bordetella pertussis* among military trainees and the evaluation of newly developed highly sensitive PCR-based beacon probe for the detection of *B. pertussis*	Whooping cough is a contagious respiratory disease caused by *Bordetella pertussis*. Studies indicate that it is on the rise in adolescents, adults, and within confined populations such as military trainees. Surveillance for *B. pertussis* is established at 4 military training centers. Specimens are evaluated using PCR-based beacon probe. Standard culture serology, and PCR results are compared to validate the accuracy of the PCR method.	Ongoing. As of September 2002 147 specimen sets have been tested. *B. pertussis* has been detected in 1% of bacterial cultures, 2% of serologic tests, and 6% of PCR tests.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
Action Item #16: Provide Healthcare System Administrators and Other Decision Makers with Data on the Impact of Drug-Resistant Organisms (e.g., Outcome, Treatment Costs) and on Effective Prevention and Control Measures.			
AHRQ	Research Demonstration (U18): Centers for Education and Research on Therapeutics (CERTs) program: a national initiative to increase awareness of the benefits and risks of new, existing, or combined uses of therapeutics through education and research.	The University of Pennsylvania Center for Education and Research on Therapeutics has undertaken studies on AR with the Veterans Affairs Medical Center in collaboration with Health Services Research and Development Service, Department of Veterans Affairs, and with hospitals in the Delaware Valley in collaboration with NIAID.	Manuscript in press: Metlay JP, Strom BL, Asch DA. Patterns of antimicrobial drug exposure and subsequent risk of trimethoprim-sulfamethoxazole-resistant urinary tract infections. J Antimicrob Chemother. Ongoing patient recruitment for study of antibiotic-resistant pneumococcal pneumonia.
Action Item #17: Expand and Enhance Coordination of Surveillance for Drug-Resistance in Enteric Bacteria In Sick and Healthy Humans and in Sick and Healthy Animals on Farms, at Slaughter, and at Retail.			
FDA	AR DNA in feed ingredients	Assess the prevalence of antibiotic-resistant DNA in feed ingredients , primarily rendered product. This work will be done in conjunction with FDA field personnel when they inspect suppliers for compliance with the bovine spongiform encephalopathy (BSE) regulation. Results will be incorporated into NARMS.	Ongoing. Survey of rendered products completed and isolation, identification, and testing of samples in process. Survey of vegetable products in planning stage.
Action Item #18: Evaluate the Usefulness of Monitoring Sentinel Human Populations (e.g., Farm, Abattoir, Fruit and Vegetable, and Food Processing Plant Workers) and Persons in the General Community for Infection or Colonization with Resistant Enteric Bacteria.			
USDA	Risk factors for microbiological contamination of produce: a field study of domestic and imported produce in packing sheds.	This funded project will look at produce grown in the U.S. an Mexico and processed in U.S. packing shed for microbial contamination. Additionally, farm workers and packing shed workers will be monitored.	Ongoing
USDA	Research Project	This project will look at transmission dynamics between animal and human populations.	Ongoing
Action Item #19: Conduct Pilot Studies To Assess the Extent of Environmental Contamination by Antimicrobial Drug Residues and Drug-Resistant Organisms That Enter the Soil or Water From Human and Animal Waste. If Contamination is Detected, Conduct Appropriate Surveillance in Waste, Surface and Ground Water, and Soil from Agricultural Areas in Which Waste Is Used for Fertilizer, and Conduct Studies To Determine Potential Impact on Human and Animal Health.			
Action Item #20: Gather Information on the Relationship Between Antimicrobial Pesticide and Herbicide Use and the Emergence of Drug-Resistance by Monitoring.			

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
USDA	See Action Item #18: Risk Factors	See Action Item #18: Risk Factors	See Action Item #18: Risk Factors
Focus Area II: Prevention and Control			
Action Item #21: Identify Factors That Promote or Impede Appropriate Drug Use in Hospitals, Extended Care Facilities, and Outpatient Settings In Collaboration with Partners.			
AHRQ	Research Program Project (P01): Understanding and eliminating health disparities in blacks, project two.	Economic access to antiretroviral (ARV) prescription drugs and adherence to ARV guidelines for African- American Medicaid enrollees with AIDS or HIV disease in South Carolina.	Medical University of South Carolina program under way to increase the number of providers treating under current guidelines.
AHRQ	Research Projects (R01): Trial to reduce antimicrobial prophylaxis errors.	The trial will assess methods to avoid mistimed administratic of preoperative antimicrobial agents.	Data collection is ongoing.
AHRQ	Research demonstration and dissemination project (R18): HIV treatment error reduction using a genotype database	This project is evaluating a computerized decision- support system that integrates HIV genotypic testing results with corresponding patient medication data within an electronic medical record system to reduce antiretroviral prescribing errors and improve antiretroviral drug selection. A second aim is to assess the efficacy and usability of this system in a community-based, outpatient setting serving a predominantly urban, minority, and low-income population.	Data to be measured and analyzed are the frequency of rules triggered, provider responses to alerts, and clinical outcomes measured by HIV viral load. Clinical outcomes will be statistically analyzed as success or failure by absolute viral load and its relative reduction. Both analyses will look at correlation of success or failure with the presence or absenc of an alert and the provider response to alerts. System usability by providers will also be assessed qualitatively.
AHRQ	Research Demonstration (U18): Centers for Education and Research on Therapeutics (CERTs) program: a national initiative to increase awareness of the benefits and risks of new, existing, or combined uses of therapeutics through education and research	The Harvard Pilgrim Healthcare CERT supports nine collaborating systems within an HMO Research Network to study antibiotic use in children.	A retrospective cohort study using automated record linkage is under way to determine rates of antibiotic use in pediatric patients and indications for therapy over time and across nin geographic regions.
CDC	See Action Item #63 (Wisconsin Antibiotic Resistance Network).	See Action Item #63 (Wisconsin Antibiotic Resistance Network).	See Action Item #63 (Wisconsin Antibiotic Resistance Network).
CDC	See Action Item #63 (The Chicago Antimicrobial Resistance Network).	See Action Item #63 (The Chicago Antimicrobial Resistance Network).	See Action Item #63 (The Chicago Antimicrobial Resistance Network).
CDC	See Action Item #63 (IMPART - Inter-Mountain Project on Antimicrobial Resistance and Therapy).	See Action Item #63 (IMPART - Inter-Mountain Project on Antimicrobial Resistance and Therapy).	See Action Item #63 (IMPART - Inter-Mountain Project on Antimicrobial Resistance and Therapy).

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
VA	Appropriate use of antimicrobials	The VHA has a national formulary, develops and implements care guidelines, and provides extraordinary educational opportunities for staff to deal with questions concerning appropriate use of antibiotics. This is an ongoing activity, but the effort will continue to be enhanced by further collaboration with federal agencies and other partners (including the privat sector) since appropriate antibiotic usage involves many components such as physician education, education of the public, appropriate drug advertising, control of over-the-counter antibiotic use, and many other items that require intervention both inside and outside of the federal systems.	Ongoing.
FDA	Labeling Rule	The new labeling is intended to educate physicians and the public about the resistance problem and to encourage physicians to prescribe systemic antibacterial drugs only when clinically necessary.	The Final Labeling Rule was published in the Federal Register on February 6, 2003. The rule will go into affect February 6, 2004.
Action Item #22: Develop Appropriate Drug Use Policies and Evaluate the Impact (Including on Prescribing Patterns, Resistance Rates, Patient Outcomes, and Cost) of Implementing These Policies in Hospitals and Other Health Care Delivery Settings. Identify Ways To Increase Adherence to Appropriate Use Policies Proven To Be Beneficial in Collaboration with Partners.			

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
AHRQ	Research Projects (R01): 1. Reducing AR: a randomized trial. 2. Otitis Media: parent education to avoid antibiotic use. 3. Pediatric Evidence based Medicine: getting evidence used at the point of care. 4. Minimizing AR in Colorado (MARC)	1. Developing and testing physician- and patient-level interventions in entire communities in a randomized trial to determine if the interventions reduce prescribing and the prevalence of resistance. Three-pronged intervention strategy: (1) direct education of parents of children under 6 years old to improve knowledge and decrease inappropriate parental demand for antibiotics, (2) targeted physician behavior change toward more judicious prescribing of antibiotics, and (3) improving general public awareness of issues of antibiotic over prescribing and resistance at the community level. 2. Randomized clinical trial to evaluate the need for antibiotic therapy during an episode of mild acute otitis media. 3. Evaluation of whether use of an evidence-based decision-support system at the point of care will reduce frequency and duration of antibiotic therapy for otitis media and reduce duration of therapy for acute sinusitis. 4. Evaluation of the independent and combined marginal impact on antibiotic prescribing behavior and antibiotic resistance.	1. Study currently in progress and should provide clinically applicable evidence that will decrease the unnecessary use antibiotics. 2. Study recently completed, and final report in preparation. 3. Christakis DA, Zimmerman FJ, Wright JA, Garrison MM, Rivara FP, Davis RL: A randomized controlled trial of point-of-care evidence to improve the antibiotic prescribing practices for otitis media in children. Pediatrics. 2001;107: E15. Stud continues in progress and will yield data on the effectiveness of providing evidence a the point of care on reducing antibiotic use. 4. Study currently in progress. Preliminary evidence of favo
AHRQ	Collaborative Agreement (U01): Practice-Based Research Network (PBRN)--Safety New Antibiotic Prescription (SNAP)	Parents of children with mild to moderate otitis media were given an antibiotic prescription but instructed not to fill it unless the child's symptoms worsened over the first 48 hours.	Significant reduction in the number of children on antibiotics without any change in outcomes.
AHRQ	Research Demonstration (U18): Centers for Education and Research on Therapeutics (CERTs) program: a national initiative to increase awareness of the benefits and risks of new, existing, or combined uses of therapeutics through education and research	The University of Pennsylvania CERT has begun studies on improving the use of antibiotics locally and nationally, on reducing the use of antibiotics for acute bronchitis in outpatients, on the effect of formulary changes on the resistance patterns of *Escherichia coli* and *Klebsiella spp.,* on antibiotic-resistance patterns from outpatients with acne who are receiving tetracycline and a group of patients who a not, on antibiotic use and infection with drug-resistant *Streptococcus pneumoniae* in the United Kingdom, on risk factors for infection due to fluoroquinolone-resistant *E. coli* and *K. pneumoniae,* on risk factors for fluoroquinolone resistance in infections due to extended-spectrum beta-lactamase-producing *E. coli* and *K. pneumoniae* and on adherence to protease inhibitors and adherence to nonnucleoside reverse transcriptase inhibitors in HIV infection.	Independent risk factors for fluoroquinolone resistance were fluoroquinolone use, aminoglycoside use, and long-term care facility residence (Clinical Infectious Diseases. 2001;33:1288-94).

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
AHRQ	Research demonstration (U18): optimizing antibiotic use in long-term care	Evaluation to determine if a clinical algorithm for managing urinary tract infections in older adults in residential long-term care facilities can reduce the overall use of antibiotics in long-term care facilities.	Loeb MB, Craven S, McGeer AJ, et al.: Risk factors for resistance to antimicrobial agents among nursing home residents. Nursing homes in Ontario and Idaho have been recruited, algorithms have been introduced, and data are being collected. Projected impact is that the rate of antibiotic prescribing at intervention sites will decrease.Am J Epidemiol. 2003; 157:40-7.
CDC	Evaluation of routine cycling of antimicrobial agents	Routine cycling in the choice of empiric antimicrobial agents has been proposed as a means of limiting development of A mutants in hospitalized patients. This study in medical intensive care units at 3 institutions evaluates changes in prevalence of resistant target pathogens and patient outcomes during cycling interventions compared to baseline. The results will indicate whether cycling interventions have a protective effect on infection or colonization with resistant target pathogens and the impact of specific cycling periods on adequate therapy for suspected infections, length of hospital stay, and mortality rates.	Data collection and isolate processing is complete. Preliminary results suggest cycling of agents are ineffective to reduce targeted resistance among gram-negative isolates. Reporting of results and suggested measures for further study or consideration for hospitals considering cycling are in progress, expected Summer 2003.
CDC	See Action Item #26 (Campaign to Prevent Antimicrobial Resistance in Healthcare Settings).	See Action Item #26 (Campaign to Prevent Antimicrobial Resistance in Healthcare Settings).	See Action Item #26 (Campaign to Prevent Antimicrobial Resistance in Healthcare Settings).
CDC	See Action Item #26 (State-based multifaceted interventions for clinicians and patients to promote the appropriate use of antibiotics for outpatient upper respiratory infections).	See Action Item #26 (State-based multifaceted interventions for clinicians and patients to promote the appropriate use of antibiotics for outpatient upper respiratory infections).	See Action Item #26 (State-based multifaceted interventions for clinicians and patients to promote the appropriate use of antibiotics for outpatient upper respiratory infections).
CDC	See Action Item #26 (Partnerships with healthcare delivery organizations and insurers to promote appropriate use of antibiotics for outpatient upper respiratory infections).	See Action Item #26 (Partnerships with healthcare delivery organizations and insurers to promote appropriate use of antibiotics for outpatient upper respiratory infections).	See Action Item #26 (Partnerships with healthcare delivery organizations and insurers to promote appropriate use of antibiotics for outpatient upper respiratory infections).
CDC	See Action Item #63 (The Chicago Antimicrobial Resistance Program (CARP).	See Action Item #63 (The Chicago Antimicrobial Resistance Program (CARP).	See Action Item #63 (The Chicago Antimicrobial Resistance Program (CARP).
VA	See Action Item #21.	See Action Item #21.	See Action Item #21.
FDA	See Action Item #21 (Labeling Rule).	See Action Item #21 (Labeling Rule).	See Action Item #21 (Labeling Rule).
Action Item #23: Evaluate the Relationship Between Prescribing Behavior and Specific Antimicrobial Drug Marketing and Promotional Practices. Assess the Public Health Effects of These Practices in Collaboration with Partners.			

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
FDA	Direct to Consumer (DTC) Promotion	Review "Direct to Consumer" (DTC) promotion as applies to antimicrobials.	Ongoing.
Action Item #24: Help Individual Hospitals and Healthcare Systems Analyze How the Availability of AR Data and Computer-Assisted Decision Support Systems Influences Prescriber Behavior, Health Outcomes, and Costs. This Plan May Include the Provision of Computer Software and the Establishment of Projects That Involve the Medicare Peer Review Organizations (PROs).			
CDC	See Action Item #63 (The Chicago Antimicrobial Resistance Project (CARP).	See Action Item #63 (The Chicago Antimicrobial Resistance Project (CARP).	See Action Item #63 (The Chicago Antimicrobial Resistance Project (CARP).
CDC	See Action Item #63 (IMPART - Inter-Mountain Project on Antimicrobial Resistance and Therapy).	See Action Item #63 (IMPART - Inter-Mountain Project on Antimicrobial Resistance and Therapy).	See Action Item #63 (IMPART - Inter-Mountain Project on Antimicrobial Resistance and Therapy).
VA	Emerging Pathogens Initiative (EPI)	Data on antimicrobial resistance with quartile rankings in the VHA nationwide are provided to the Networks, including reporting site-specific data by using the EPI, an automated surveillance system. This will be an ongoing initiative since it is not entirely clear what the best method for AR feedback w be in the final analysis.	Ongoing at VA sites across the country. There is an updated version in final stages for implementation that includes antibiotic resistant organisms.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
**** TOP PRIORITY **** **Action Item #25: Conduct a Public Health Education Campaign To Promote Appropriate Antimicrobial Use as a National Health Priority. The Health Campaign Should Involve Many Partners.**			
CDC	National advertising campaign promoting the appropriate use of antibiotics	This national media education campaign is being developed to promote appropriate antimicrobial drug use in the community for upper respiratory infections, e.g., to decrease patient requests for antibiotics for illnesses for which they offer no benefit. Target audiences are parents of young children and healthy adults. The campaign will use a variety of health communication materials based on concepts tested in focus groups, and its effectiveness will subsequently be evaluated.	Ogilvy Public Relations Worldwide was awarded the contract in September 2001. Phase I of the campaign was launched during 2002 which focused on developing concepts for the campaign. Throughout the year these concepts were tested on eight focus groups and results were used to develop a strategic communication plan in preparation for full scale, nation-wide launch (Phase II) scheduled for September 2003
CDC	See Action Item #26 (State-Based Multifaceted Interventions and Council for Affordable Quality Healthcare).	See Action Item #26.	See Action item #26.
FDA	Education/outreach plan	Education/Outreach plan regarding appropriate use of antimicrobials for consumers, health professionals, and health educators (includes website) (timeline 6-12 months)	The FDA-CDC education/outreach project is in the later phases of development with a launch date scheduled for September 14, 2003, with an exhibition planned at the 43rd Interscience Conference on Antimicrobial Resistance and Chemotherapy (ICAAC) in Chicago, IL.
FDA	See Action Item #23 (Direct to Consumer (DTC) Promotion).	See Action Item #23 (Direct to Consumer (DTC) Promotion).	See Action Item #23 (Direct to Consumer (DTC) Promotion).
**** TOP PRIORITY **** **Action Item #26: In Collaboration with Many Partners, Develop and Facilitate the Implementation of Educational and Behavioral Interventions That Will Assist Clinicians in Appropriate Antimicrobial Prescribing.**			

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
AHRQ	Independent Scientist Award (K02): shared decision-making and inappropriate antibiotic use	The recipient will continue to expand what is known about pediatric quality of care assessment and improvement and to translate this knowledge into practice, focusing on antibiotic prescribing for respiratory infections in children. Understanding how doctor-parent communication affects clinical decision-making around antibiotic prescribing will facilitate the development of a quality improvement intervention to address this problem. This study focuses on doctor-parent communication as a determinant of both inappropriate antibiotic prescribing and parent satisfaction with care. Parents presenting with their children who were suffering from cold symptoms were recruited for study participation. With informed consent, both physicians and parents were surveyed and their encounters were videotaped.	Ongoing analyses of these data involve an in-depth assessment of the patterns of communication between the physicians and parents observed in the 570 pediatric acute care encounters. The findings from this work will be used to develop a communication-based intervention to decrease antibiotic over-prescribing in the pediatric outpatient setting.
AHRQ	Mentored Clinical Scientist Award (K08): shared decision-making and inappropriate antibiotic use	The recipient will develop and validate an instrument to measure shared decision-making in pediatric primary care. This instrument will then be used in a cross-sectional study t examine the relationship of shared decision-making to quality of care outcomes for children's upper respiratory infections. The candidate hypothesizes that shared decision-making in acute primary care visits for upper respiratory infection will decrease inappropriate antibiotic prescribing, while preservir visit satisfaction.	The award supports a graduate student at the University of Wisconsin to facilitate her acquisition of advanced research competencies in the science of interpersonal communication in clinical settings, including completion of a Ph.D. in Population Health, training in analysis of communication during medical interactions.
CDC	Campaign to prevent antimicrobial resistance in healthcare settings	This campaign focuses on preventing AR in healthcare settings, such as hospitals and long-term care facilities. An evidence-based 12-step program promotes four strategies for clinicians: 1) preventing infection, 2) diagnosing and treating infection effectively, 3) using antimicrobials wisely, and 4) preventing transmission. Variations of the 12 steps will be tailored to specific patient populations (e.g., dialysis, surgery, geriatrics, critical care, obstetrics, emergency care, pediatrics, and patients in long term care facilities). When these strategies are fully implemented and evaluated, improvements are anticipated in infection control, appropriate antimicrobial drug use and incidence of drug-resistant infections occurring in healthcare settings.	Established partnerships with Infectious Diseases Society of America (IDSA) and American Society of Microbiology (ASM to disseminate campaign messages; developed initial educational materials for clinicians; created website; rolled out campaign and launched a 12-step campaign specifically for dialysis patients in 2002. Design of 12-step campaign for preventing AR in surgery patients is underway utilizing collaborations with the American College of Surgeons (ACS) and the Surgical Infection Society (SIS), as well as a campaign for hospitalized children. Launch of both is expected this Fall 2003. Several health communication tools were developed and disseminated to various health systems including brochures, slide sets, posters, pockets cards, and badge. Four institutions in Pittsburgh piloted the campaign materials and conducted an evaluation.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CDC	State-based multifaceted interventions for clinicians and patients to promote the appropriate use of antibiotics for outpatient upper respiratory infections	The campaign assists states in implementing broad-based health communication and behavioral interventions to promo appropriate antibiotic use for outpatient upper respiratory infections. State health departments develop broad-based coalitions (e.g., state medical societies, healthcare delivery organizations, healthcare purchasers, consumer groups), us CDC educational materials, develop materials of their own, and launch campaigns targeting providers and the general public. Controlled trials have demonstrated success of this program in decreasing inappropriate prescribing; also, nationwide antibiotic prescribing rates for children are declining.	Ongoing in twenty-seven states. In November 2002 the campaign held, with the California Medical Association, a national appropriate antibiotic use conference in Sacramento, CA. The fourth national conference, "Expanding Our Vision: CDC and Partners' National Conference on Appropriate Antibiotic Use in the Community" will be held June 5-7, 2003 The Campaign provides technical assistance through monthly phone calls with state partners. The National Campaign is developing an evaluation manual for state partners as a guide for developing and implementing impact and/or outcome.
CDC	Partnerships with healthcare delivery organizations and insurers to promote the appropriate use of antibiotics for outpatient upper respiratory infections	Work with Coalition for Affordable Quality Healthcare to implement educational and behavioral interventions for clinicians and patients to promote the appropriate use of antibiotics for outpatient upper respiratory infections in managed care organizations.	Continued projects in twent-six organizations, with 131 millio members in 2002. Implemented CME certification programs for healthcare personnel participating in educational programs.
CDC	A medical curriculum promoting appropriate use of antibiotics	Topics include extent of antibiotic resistance, diagnostic techniques, and appropriate antibiotic use. Case studies focus on examination, diagnosis, treatment, and communication. This course is designed to meet the needs of a variety of medical schools with components that can be used separately or as a whole.	During 2001, produced multi-faceted educational design for the curriculum. During 2002 CDC, in collaboration with the Association of American Medical Colleges, recruited medical schools to participate in a pilot testing of the medical school curriculum. Results from the pilot will help in the development of appropriate evaluation tools, in the evaluation of the curriculum in terms of acceptability of the material and feasibility of implementation, in the determination of appropriate packaging and marketing to appropriate target audiences, and in final revisions.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CDC	Reporting antimicrobial susceptibility data to clinicians	Assist NCCLS to produce guidelines for clinical microbiology labs on how to compile and report summaries of cumulative antimicrobial susceptibility data (antibiograms) in a standardized manner to aid in clinical decisions. When completed and evaluated, standard reports should improve empiric prescribing, based on data of antimicrobial susceptibility testing and allow comparisons of data among hospitals.	Developed guidelines in 2001.
DoD	Development of an intervention to enhance the communication skills of primary care providers on the prudent use of antimicrobials	A workshop for enhancing healthcare provider communication skills in advising patients on the prudent use of antimicrobial agents. Workshop materials include 1) a video illustrating doctor-patient discussions on inappropriate antimicrobial usages; 2) a booklet containing recommendations on applicable communication techniques; and 3) a workshop agenda, syllabus, and other supporting materials. The result of the workshop is a heightened ability to manage discussions with patients on prudent antimicrobial use. Workshop effectiveness will be evaluated by an analys of workshop participant questionnaires completed at the end of the workshop; a follow-up survey on participant perceptior about improvements in communication skills, success in influencing patient demand for antimicrobial agents, and use of patient education materials on the prudent use of antimicrobial agents; and a review of pre- and post-workshop antimicrobial prescribing rates by participating primary care providers; and assessment of training effectiveness.	Existing and relevant educational programs and materials appropriate for the DoD health care setting are identified. A pilot training program will be implemented this year.
VA	Prudent use of antibiotics interventions	The VHA is already involved in many of these activities with particular emphasis on educational activities and training for prescribers at all levels, including physicians, nurse practitioners, and others who are involved with the direct care of patients. Particularly, the VHA provides a strong role in education for health professions students, medical and nursing trainees, and others critical to the provision of care to patients such as social workers, psychologists, and advance role nurses. In addition, the VHA has produced guidelines, including those that relate to antimicrobial drug use. Therefore, the VHA is well underway for this action item.	Ongoing.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
FDA	See Action Item #23 (Direct to Consumer (DTC) Promotion).	See Action Item #23 (Direct to Consumer (DTC) Promotion).	See Action Item #23 (Direct to Consumer (DTC) Promotion).
FDA	See Action Item #25 (Education/Outreach Plan) .	See Action Item #25 (Education/Outreach Plan) .	See Action Item #25 (Education/Outreach Plan) .
Action Item #27: Explore Ways To Integrate Appropriate Use Information into Antimicrobial Package Inserts and Promotional Materials, To Provide Such Information to Patients with Each Prescription, and To Provide Clear Guidance to Industry To Ensure That Promotion of Antimicrobials Directed Towards Consumers Encourages Appropriate Use and Discourages Inappropriate Use.			
FDA	See Action Item #21 (Labeling Rule).	See Action Item #21 (Labeling Rule).	See Action Item #21 (Labeling Rule).
Action Item #28: Articulate Factors That Support the Current Approach of Requiring Prescription-Only Dispensing for All Systemic (e.g., Nontopical) Antimicrobial Drugs Used In Clinical Medicine.			
Action Item #29: Periodically Review and Update Antimicrobial Drug Susceptibility Information Including In Drug Labeling, with Input from Stakeholders and Other Experts, e.g., the National Committee for Clinical Laboratory Standards (NCCLS) and CDC.			
FDA	See Action Item #21 (Labeling Rule).	See Action Item #21 (Labeling Rule).	See Action Item #21 (Labeling Rule).
Action Item #30: Convene an Advisory Panel or Other Expert Group in Involving Stakeholders and Partners To Consider Issues Related to Resistant Pathogens That Cause Serious Infections for Which Available Treatments Options Are Very Limited or Nonexistent.			
FDA	See Action Item #21 (Labeling Rule).	See Action Item #21 (Labeling Rule).	See Action Item #21 (Labeling Rule).
FDA	Otitis Media Advisory Committee	Discussion of clinical study design for drugs treating acute otitis media (which may impact resistance in the pediatric population).	Meeting held on July 11, 2002.
FDA	FDA/PhRMA Co-Sponsored Workshop	Discussion of statistical issues in clinical trials including trials related to resistant pathogens.	Meeting held on November 9, 2002.
FDA	FDA/IDSA/PhRMA Co-Sponsored Public Workshop	Coordinated and hosted a public workshop that brought together top national leaders and scientists from the Infectious Disease Society of America, Pharmaceutical Research and Manufacturers of America, and U.S. academic institutions along with representatives from CDC and NIH to address current topics of interest associated with AR and antimicrobial drug development.	Meeting held on November 19-20, 2002.
FDA	Anti-Infective Drugs Advisory Committee (ADAC)	Discussion of issues relating to macrolide-resistant *Streptococcus pneumoniae* (MRSP)	Meeting held on January 24, 2003.
FDA	Anti-Infective Drugs Advisory Committee (ADAC)	Discussion of issues relating to AR in*Streptococcus pneumoniae*.	Meeting held on March 4, 2003.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
FDA	Anti-Infective Drugs Advisory Committee (ADAC)	Discussion of a list of Antimicrobial Resistant Pathogens of Public Health Importance to assist stakeholders in the development of antimicrobial drugs related to resistant pathogens.	Meeting held on May 5, 2003.
Action Item #31: Convene A Working Group To Examine the Impact of Federal Reimbursement Policies for Home Parental Antimicrobial Treatment, Appropriate Antimicrobial Use, and Appropriate Use of Antimicrobial Susceptibility Testing. Where Needed, the Working Group Will Make Recommendations for Modifying These Policies.			
Action Item #32: Develop and Submit Measures for Appropriate Antimicrobial Use to the National Committee for Quality Assurance for Inclusion in Health Plan Employer Data and Information Set (HEDIS), Which Provides Comparative Data on Managed Care Organizations			
CDC	Development and testing of HEDIS measures for appropriate antibiotic use	In this project, CDC epidemiologists collaborate with experts in the development and testing of HEDIS measures to develop and test one or more measures of appropriate antimicrobial use in children. Potential measures include rates of prescribing antimicrobial drugs for acute upper respiratory infections and bronchitis; rate of prescribing antimicrobial drugs for pharyngitis where no throat culture or rapid streptococcal antigen test was performed; and episodes of otitis media treated with a recommended first-line agent. If the measure is incorporated into HEDIS, the measure and its impact on physician and patient awareness of appropriate antimicrobial use will be evaluated.	Ongoing. Awarded contract in 2001 to Association of American Medical Colleges. In 2002, National Center for Quality Assurance (NCQA) was presented with specifications for two potential measures relating to Appropriate Antibiotic Prescribing for Respiratory Infections for Children. NCQA accepted the measures into the HEDIS set for 2004.
Action Item #33: Evaluate The Potential Impact Of Improved Diagnostic Tests, Including Rapid Point-of-Care Tests on Antimicrobial Drug Use and Patient Care, and Assess Their Financial Implications. Take into Account Tests That Distinguish Between Bacterial and Viral Infections, Tests That Identify Resistant Pathogens, and Tests That Distinguish Common Clinical Entities such as Bacterial Sinusitis and Acute Bacterial Otitis Media from Illnesses with Similar Manifestations for Which Antimicrobials Are Not Beneficial.			
AHRQ	Small research grant (R03): a diagnostic decision aid (DDA) for pediatric sinusitis.	Investigators at the University of Washington are exploring whether use of a diagnostic decision aid that is completed by parents in the waiting room prior to being seen can assist providers in more accurately diagnosing sinusitis and thereby diminish inappropriate antibiotic use.	A randomized controlled trial using wireless hand-held computers is under way in a university-based clinic to see whether a DDA can prove useful to providers and whether it can be integrated into a wireless computerized clinical information system.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CDC	Rapid detection of MRSA colonization to reduce spread within hospitals	This project's focus has been revised to study the dynamics of MRSA transmission in the ICU setting. This information will the be used to institute appropriate infection control measures to decrease the spread of MRSA in high-risk hospital areas.	Continued patient enrollment in 2003. Samples have been collected and stored to determine strain transmission.
Action Item #34: Identify Economic and Other Barriers in the Health Care System (e.g., Reimbursement Policies by Third Party Payers, Managed Care Practices, Cost Considerations, Empiric Treatment Recommendations, etc.) to Diagnostic Testing That Promotes Appropriate Use of Antimicrobials. Develop Recommendations That Remove Disincentives or Promote Incentives to Such Testing.			
VA	Laboratory accreditation	The VHA currently participates in surveys by the College of American Pathologists and all VHA laboratories are appropriately credentialed.	Ongoing.
Action Item #35: In Collaboration With Professional Societies, Industry, Health Departments, And Other Stakeholders And Partners, Develop Guidelines for Clinicians And Clinical Microbiology Laboratories To Address Appropriate Specimen Collection, Interpretation, And Reporting Of Susceptibility Tests, And Use Of In-Office Tests For Infection.			
CDC	National laboratory system demonstration projects	These projects promote linkages and coordination between State Public Health and clinical microbiology laboratories to optimize laboratory practice, in collaboration with medical societies and other stakeholders. AR is a major focus area. Example: In one project, the State of Washington developed and distributed a survey of laboratory practices related to antimicrobial susceptibility testing (AST) and has provided training to approximately 2,000 laboratorians in a dozen stat in quality control for AST testing through a teleconference and a train-the trainer program on using an interactive CD-ROM program on the NCCLS AST laboratory guidelines. Th survey will then be re-administered to measure changes in practice and use of the guidelines.	CDC-funded demonstration projects are underway in numerous states. MASTER is an acronym for Multi-level Antimicrobial Susceptibility Testing Educational Resources. Periodic updates on the website provide case studies addressing contemporary testing issues, questions and answers for users, a review of recent papers that have implications for testing and reporting, other new information, and lists of reference materials including books, and links to other websites. National Laboratory Training Network sponsors courses in how to use NCCLS standards, including new information included in the 2003 standards and the importance of using antibiograms.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CDC	Grant Program: Applied Research on Antimicrobial Resistance - Validation of National Committee for Clinical Laboratory Standards (NCCLS) Breakpoints for Bacterial Human Pathogens	The purpose of the program is to provide assistance for applied research aimed at prevention and control of the emergence and spread of AR in the United States. This program will focus on validation of NCCLS breakpoints for bacterial human pathogens of public health importance. This research includes three components that will provide information needed to prevent and control AR: (1) validating existing interpretive criteria for pathogens of public health importance; (2) developing new interpretive criteria for pathogens of public health importance using existing NCCLS methods and quality control; and (3) developing new interpretive criteria and new antimicrobial susceptibility testin methods for pathogens of public health importance using existing NCCLS methods and quality control as a starting point for novel test development.	Funded three programs in the Fall of 2002: University of Texas Medical Center, (Development of Interpretive Breakpoint Criteria for*Neisseria Meningitidis*); University of Pittsburg, (NCCLS Interpretive Criteria for Salmonella); University of Wisconsin Medical Center, (Validation of NCCLS Methods and Breakpoints for Extended Spectrum beta-lactamases). First year progress reports expected Fall 2003.
CDC	See Action Item #26 (State-based multifaceted interventions for clinicians and patients to promote the appropriate use of antibiotics for outpatient upper respiratory infections).	See Action Item #26 (State-based multifaceted interventions for clinicians and patients to promote the appropriate use of antibiotics for outpatient upper respiratory infections).	See Action Item #26 (State-based multifaceted interventions for clinicians and patients to promote the appropriate use of antibiotics for outpatient upper respiratory infections).
Action Item #36: In Collaboration with Professional Societies, Industry, Health Departments, and Other Stakeholders, Develop Guidelines That Address the Use of Clinical Microbiology Laboratories for Use by Health Care Delivery Organizations.			
Action Item #37: Promote the Increased Performance of Direct Examination of Microbiological Specimens (e.g., by Gram Stain or Other Rapid Method) in Circumstances Where Appropriate, Clinically Relevant, and Reliable Information Can Be Garnered, as Readily Available Point-of-Care Diagnostic Test. This Step Will Require Working Within the Framework of the Clinical Laboratory Improvement Amendment (CLIA) Regulations and Involving Medical Education And Health Care Delivery Organizations.			
Action Item #38: Identify Factors That Promote Transmission of Drug-Resistant Pathogens in Healthcare Facilities, in Extended Care Facilities, and in Community Settings, Including Daycare Centers in the Community at Large. These May Include Characteristics of the Facilities and of the Populations They Serve.			
CDC	Grant Program for Applied Research on Antimicrobial Resistance: Microbiologic Mechanisms of Dissemination of AR Genes and Relationship to Antimicrobial Drug Use	Awards for projects to develop information necessary to prevent and control the emergence and spread of resistance in selected bacteria through better understanding the mechanisms through which resistance develops and spreads in field settings.	Three three-year awards were made in 2001. Research areas included AR among*E. faecium* in animal and human populations and fluoroquinolone resistance among*E. coli* in healthcare settings.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CDC	Grant Program for Applied Research on Antimicrobial Resistance: Characterization of Strains of Communit Associated Methicillin-Resistant *Staphylococcus Aureus*	Awards will be made to applicants who assemble a network of partners who identify and access a defined population of persons within which there is community-associated MRSA disease and data sufficiently prevalent to allow appropriate analyses; who obtain strains of *S. aureus* causing disease in this population with appropriate epidemiologic and clinical data to make findings generalizable to similar populations from diverse geographic areas; and who characterize strains and/or the relationship between these strains using a variety of molecular and biochemical techniques.	Awards will be made in September 2003.
CDC	Antimicrobial resistance in *Staphylococcus aureus* and *Streptococcus pneumoniae* among Alaska Natives	CDC is conducting surveillance and evaluation of prevention and control measures for MRSA skin infections, community-wide surveys for carriage of penicillin-nonsusceptible *Streptococcus pneumoniae*, and surveys on antimicrobial drug use. These activities will provide knowledge of MRSA prevalence and effectiveness of prevention measures, assist with the development of treatment guidelines for community-onset MRSA infections, assess the effect of the new pneumococcal vaccine on resistant pneumococcal infections, and assess the effect of education on appropriate antimicrobial agent use in Alaska.	New data from this work show a decrease in colonization wit antibiotic resistant *S. pneumoniae* following use of the new pneumococcal vaccine, and a 30% decrease in antibiotic use after education on appropriate antimicrobial agent use in Alaska.
CDC	See Action Item #39 (Centers of Excellence in Healthcare Epidemiology).	See Action Item #39 (Centers of Excellence in Healthcare Epidemiology).	See Action Item #39 (Centers of Excellence in Healthcare Epidemiology).
CDC	See Action Item #63 (The Chicago Antimicrobial Resistance Project CARP).	See Action Item #63 (The Chicago Antimicrobial Resistance Project CARP).	See Action Item #63 (The Chicago Antimicrobial Resistance Project CARP).
CDC	See Action Item #63 (The Wisconsin Antibiotic Resistance Network).	See Action Item #63 (The Wisconsin Antibiotic Resistance Network).	See Action Item #63 (The Wisconsin Antibiotic Resistance Network).

**** TOP PRIORITY ****

Action Item #39: Evaluate the Effectiveness (Including Cost-Effectiveness) of Current and Novel Infection-Control Practices for Health Care and Extended Care Settings and in the Community. Promote Adherence to Practices Proven To Be Effective.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CDC	Centers of excellence in healthcare epidemiology (Prevention Epicenters)	Academic medical centers conduct research to improve infection control practices. Current projects address prevention of infections related to central vascular catheters and surgical site and bloodstream infections. A substantial proportion of these infections are drug-resistant. Reduction of these infections would also reduce antimicrobial use in healthcare settings, thus decreasing the environmental pressure favoring development and spread of resistant infections.	Awarded funds to seven academic medical centers for research projects in 2001. During 2002, survey was performed to determine the prevalence of central lines in adult inpatient beds in six of the seven Epicenter hospitals. Abstract reported wide variability in implementation of recommended guidelines. Data collection continued on in-hospital surveillance for surgical site infections and prevention of bloodstream infections (BSI), and implementation of a package of BSI prevention measures began. Manuscript in preparation.
CDC	See Action Item #63 (Comprehensive Demonstration Project: Building Regional Coalitions to Prevent Methicillin-Resistant *Staphylococcus aureus* (MRSA) in Healthcare Facilities,	See Action Item #63 (Comprehensive Demonstration Project: Building Regional Coalitions to Prevent Methicillin-Resistant *Staphylococcus aureus* (MRSA) in Healthcare Facilities,	See Action Item #63 (Comprehensive Demonstration Project: Building Regional Coalitions to Prevent Methicillin-Resistant *Staphylococcus aureus* (MRSA) in Healthcare Facilities.
VA	Outcome effectiveness: tuberculosis, legionella	The Infectious Diseases Program Office continues to evaluate impact on infection control and educational efforts to prevent healthcare-associated and community-based infections in the veteran population served. Specific reference can be made to the VA program to combat tuberculosis and multidrug-resistant tuberculosis as a program in which intervention was defined and outcome assessed by using statistical analysis to provide objective outcome data.	Ongoing. Roselle GA, Danko LH, Kralovic SM, Simbartl LA, Kizer KW. Tuberculosis in the veterans healthcare system: a six-year review and evaluation of programme effectiveness. Epidemiol Infect. (2000), 125, 315-323. Roselle GA, Danko LH, Kelly AA, Simbartl LA, Kralovic SM. Legionella in the Department of Veterans Affairs Veterans Health Administration (VHA): the outcome of intervention ov eight years. Abstract presented at the 39th Annual Meeting of the Infectious Diseases Society of America, October 25-28, 2001, San Francisco, CA. AA Kelly, LH Danko, SM Kralovic, LA Simbartl, GA Roselle. Legionella in the Veterar Healthcare System: Report of an Eight-year Survey In Press in Epidemiol Infect
Action Item #40: Evaluate the Cost-Effectiveness and Impact on Patient Care and Drug Resistance of Medical Devices That Incorporate Anti-Infective Compounds To Prevent Infection (e.g., Anti-Infective Urinary Catheters and Prosthetic Heart Valves). Where Appropriate (e.g., Shown To Be Effective and Not Induce Resistance), Encourage the Clinical Use of These Devices.			
FDA	Devices containing antimicrobials – draft guidance	Draft guidance document for industry: how CDRH intends to regulate devices containing antimicrobial drugs, and what information regarding efficacy and resistance CDRH wants t see in premarket applications (interim until rulemaking is completed)	In development.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
FDA	Standards development seminar	Standards development: seminar to gather information from experts on developing test methods that should/could be used to demonstrate efficacy of antimicrobial agents on devices for use in guidance and rulemaking.	Seminar held on December 3-4, 2001.
Action Item #41: Encourage the Development and Implementation of Clinical Alternatives to Those Invasive Medical Procedures That Increase the Risk of Infection in Hospitals and Other Health Care Settings, e.g., Substitutions of Transcutaneous Monitoring of Blood Oxygen Levels of Indwelling Catheters.			
Action Item #42: Evaluate the Benefits and Risks of Incorporating Antimicrobial, Disinfectant, or Antiseptic Chemicals into Consumer Products (e.g., Soap, Toys, Kitchen Utensils, Clothes, Paints, Plastics, and Film Preservatives) and of Applying Disinfectants and Sanitizers to Hard, Non-porous Surfaces such as Food-Contact Surfaces, Hospital Premises, Bathrooms, etc. Consider Whether They Have Any Efficacy in Reducing and/or May Play a Role in Promoting Drug Resistance.			
Action Item #43: Conduct a Public Health Campaign To Promote Hand Hygiene and Other Hygienic Practices, as well as Other Behaviors That Prevent the Transmission of Infectious Organisms, in Collaboration with Professional Societies and Stakeholders. This Campaign May Be Coordinated with the Public Health Education Strategy To Promote Appropriate Antimicrobial Use Described in Action Item #25: Prevention and Control.			
Action Item #44: Facilitate and Support the Activities of Infection Control Programs in Health Care Settings as a Component of Medical Care. Promote Infection Control Education at all Stages of Training and Practice for all Health Care Workers Who Have Contact with Patients.			
CDC	Division of Healthcare Quality Promotion (DHQP), National Center for Infectious Diseases (NCID)	DHQP, formerly known as the Hospital Infections Program, has in its mission surveillance, applied research, and prevention and control of infections in healthcare settings.	Numerous ongoing projects in collaboration with partners.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
VA	Educational activities since January 2001: A. Department of Veterans Affairs Occupational Safety and Health Conference, Las Vegas, NV, August, 8, 2001. B. Department of Veterans Affairs Occupational Safety and Health Conference, Las Vegas, NV, August, 9, 2001. C. Emerging Pathogens Satellite Broadcast, September 5, 2001 D. Infomercials taped and aired on VA Knowledge Network. Viewed by VHA employees.	Conference Speakers: A. Employee Health: Vaccine and PPD Issues. Speaker: Gary A. Roselle, M.D. B. Emerging Infectious Diseases. Speaker: Stephen M. Kralovic, M.D. C. Part 1 – Tuberculosis. Part II – Implementation Thoughts and the Future. Presenter: Gary A. Roselle, M.D. D. 2-3 minute "infomercials" covering issues relating to influenza, PPD's and bloodborne pathogens.	The VHA is currently in the forefront of infection control programs in the healthcare settings in the U.S. This includes national guidance, educational activities, and current financial support of the program nationwide. It is anticipated that such activities will continue, particularly because of the more recent emphasis on patient safety and infection control as part of an overall safety program to prevent excess infections in the healthcare setting.
Action Item #45: Support Ongoing Public Health Education Campaigns on Food Safety, such as FDA and USDA's Fight BAC Program, Whose Aims Are To Educate Food Producers, Retailers, and Consumers About Food Safety Practices That Reduce Foodborne Infections (Including AR Infections).			
USDA	Food Safety Education for the Hard-to-Reach and Underserved Communities	Alabama A & M University researchers will plan and implement a comprehensive, interactive food safety educatio program for small fruit and vegetable growers, reducing the potential for foodborne illness in hard-to-reach and underserved rural communities in Alabama and Tennessee.	Ongoing. Chemezi, Alabama A & M University.
USDA	Food Safety Practices and HACCP (Hazard Analysis and Critical Control Point) Implementation in Assisted Living for the Elderly	S. Iowa State University will assess food safety practices and HACCP implementation in assisted living programs for the elderly.	Ongoing. Gilmore, S. Iowa State University.
USDA	Food Safety Education for the Prevention of Foodborne Illness Among U.S. Residents 65 and Older	Kansas State University will assess food handling practices and develop a food safety education program for high-risk older adults.	Ongoing. Gordon, Kansas State University.
USDA	Food Safety Education in the 21st Century: Improving the Process	North Dakota State University will conduct research on reducing the risk of foodborne illness outbreaks among high-risk audiences through existing public education programs	Ongoing. Garden-Robinson, North Dakota State University.
USDA	Integrated Approach to Identification of Problem Food Safety Behaviors and Customized Educational Delivery for Improving Them: A Tri-State Project for South Carolina, Georgia and North Carolina	Clemson University researchers will identify unsafe food safety behaviors and develop educational programs addressing those behaviors for non-English speaking groups and hard to reach audiences.	Ongoing. Hoyle, Clemson University.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
USDA	Children Fight BAC!: A Scientific, Interactive Food Safety Instruction Program	Utah State University will use instructional computer simulation modules to teach students about the science behind the USDA's Fight BAC! public education program, while encouraging them to adopt recommended food safety behaviors.	Ongoing. Mendenhall, Utah State University.
Action Item #46: Educate the Public About the Merits and Safety of Irradiation as One Tool To Reduce Bacterial Contamination of Food.			
Action Item #47: Support Community-Based Programs That Promote and Facilitate Availability of Recommended Vaccinations for Adults and Children.			
CDC	National Immunization Program (NIP)	NIP's mission is to reduce disease and disability from diseases that can be prevented through immunization.	Numerous ongoing projects support state and community-based programs that promote vaccination and provide vaccines.
CMS	CMS's National Influenza and Pneumococcal Campaign	Mission is to improve the rates of immunization among underserved populations.	Numerous ongoing projects to support community based programs that promote adult vaccinations.
Action Item #48: Identify Vaccines Useful in Preventing Drug-Resistant Infections and Reducing Antimicrobial Drug Use and Evaluate Novel Methods For Improving Coverage with These Vaccines.			

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CDC	Measuring the effectiveness of pneumococcal conjugate vaccine for children: assessing the impact on drug-resistant *Streptococcus pneumoniae* (DRSP)	A 7-valent conjugate vaccine for *Streptococcus pneumoniae*, licensed by the FDA in 2000, is recommended by the Advisory Committee on Immunization Practices for children <5 years. Three CDC projects assess the effectiveness of this vaccine in preventing pneumococcal infections, including drug-resistant infections. One project is a case-control study of vaccine effectiveness in preventing invasive infections in children in nine Emerging Infections Program areas in which population-based active surveillance is conducted. The second project assesses impact on nasal colonization of children living in Anchorage, Alaska, through annual culture surveys. The third is a community-wide study of colonization in remote Alaska villages before and after introduction of the vaccine to assess the impact of the vaccine on carriage of drug-resistant strains among vaccinees and non-vaccinees. Data from these studies will be used to evaluate vaccine recommendations in the U.S. Decision makers in other countries will use this data to determine if pneumococcal conjugate vaccine should be used.	Ongoing. During 2000 and 2001 the study protocol was developed, a pilot study was launched, and procedures manuals and tracking system were revised in preparation for the main study. During 2002, cases and controls were enrolled and main data collection began. Interim analysis indicates that the vaccine is very (>90%) effective against disease caused by pneumococcal serotypes in the vaccine and serotypes closely related to those in the vaccine. (Whitney CG, et al.; Decline in invasive pneumococcal disease after the introduction of protein-polysaccharide conjugate vaccine. N Engl J Med 2003 May 1;348(18):1737-46).
VA	Improve use of vaccines related to prudent use of antibiotics	Department of Veterans Affairs, Veterans Health Administration Directive 2001-053. Influenza Vaccine – Recommendations for 2001-2002. Published and placed on VA Intranet website August 28, 2001. Infomercials were aired on VA Knowledge Network regarding influenza vaccine. Performance Measurement Program, 2001 and 2002 VHA Performance Measurement System Technical Manuals list Influenza Immunization and Pneumococcal Immunization as Preventive Care Quality Performance Measures, with specific recommendations for these immunizations for Nursing Home Care Units within the VHA system. Influenza Vaccine - Recommendations for 2002-2003, Veterans Health Administration Directive 2002-044, Published on 7/29/02. Domestic Hot Water Temperature Limits, Veterans Health Administration Directive 2002-073.	The VHA is already in the forefront of immunization practices as is evidenced by the pneumococcal and influenza vaccine usage rates compared to the national averages. In addition, influenza vaccine use increases each year in the VHA as emphasis on this program continues. Therefore, this action item is already under way and will continue to be an area of emphasis area for the VA.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
FDA	*H. influenzae* type B (HIB) vaccine	Monitoring of polysaccharide conjugatedvaccines, including regular inspections of the production facilities, review and conduct of Lot Release studies, and review of amendments to the current Biologic License Application	Ongoing. Several licensed vaccines. Continued vaccine supply essential to maintaining the near elimination of resistant *H. influenzae* disease in the U.S.
FDA	Pneumococcal vaccine	Monitoring and guidance provided to current manufacturer of a seven-valent conjugate vaccine. Also, provide regulatory review, conduct research and provide guidance to support licensure of additional pneumococcal vaccines (various products under IND)	Ongoing. One licensed polysaccharide and one licensed conjugate vaccine for the prevention of invasive disease and acute otitis media. Studies suggest decrease in AR among *S. pneumonia* isolates coincident with wide spread use of conjugate vaccine in infants.
FDA	Pneumococcal conjugate vaccine	Identify mechanisms for establishing efficacy of additional pneumococcal conjugate vaccines.	Workshop held to discuss serologic correlates of protection. Research regarding serologic assessment of response to vaccines ongoing.
FDA	Influenza vaccine	Regulatory and research support of annual influenza vaccine development, production and licensure, including additional manufacturers and novel technologies.	Ongoing regulatory review, research support and guidance for both current vaccines and those vaccines under IND.
Action Item #49: Evaluate the Nature and Magnitude of the Impact of Using Various Antimicrobial Drugs as Growth Promotants in Different Species, Using Current Animal Husbandry Practices. Use This Information To Assist in Risk-Benefit Assessments of Such Use.			
CDC	See Action Item #50 (Reducing resistant bacteria in food animals).	See Action Item #50 (Reducing Resistant Bacteria in Food Animals).	See Action Item #50 (Reducing Resistant Bacteria in Food Animals).
Action Item #50: Conduct Additional Research To Further Define the Effects Of Using Various Veterinary Drugs on the Emergence of Resistant Bacteria That Infect or Colonize Food Animals of Different Species, Using Various Animal Husbandry Practices. Identify Risk Factors and Preventive Measures to Humans.			
CDC, FDA	Reducing resistant bacteria in food animals	Projects assess the impact of antibiotic use in swine and cattle, develop alternatives to the use of antimicrobial drugs as growth promotants, and evaluate new practices to reduce resistant bacteria in food animals.	Awarded cooperative agreements to four schools of veterinary medicine (two for studies in dairy cattle, two in swine).
USDA	Antimicrobial Drug Use and Veterinary Costs in US Livestock Production	Report that evaluated the risks/benefits of antimicrobial drug use in livestock production.	Released May 2001.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
USDA	See Action Item #55 (Comparison of antimicrobial resistance in Salmonella,*E. coli*, and Campylobacter isolated from swine farms using different antibiotic regimens, in collaboration with University of Georgia)	See Action Item #55 (Comparison of antimicrobial resistance in Salmonella,*E. coli*, and Campylobacter isolated from swine farms using different antibiotic regimens, in collaboration with University of Georgia)	See Action Item #55 (Comparison of antimicrobial resistance in Salmonella,*E. coli*, and Campylobacter isolated from swine farms using different antibiotic regimens, in collaboration with University of Georgia)
Action Item #51: Conduct Epidemiologic And Laboratory Studies To Assess the Risk of Development and Transfer of Resistance Related to The Use of Antimicrobial Drugs in Food and Non-Food Plants, and Identify Risk Factors and Potential Preventive Measures.			
CDC	Antibiotics used as pesticides in orchards	Apple and pear orchard farmers have used streptomycin to control the plant disease fireblight, a bacterial infection caused by *Erwinia amylovora*, since the 1950s. After years of streptomycin use, streptomycin-resistant strains of *E. amylovora* developed. Farmers now use oxytetracycline in *E. amylovora* resistant areas to control fireblight. In this pilot study involving 4 orchards in 3 states, fruit is tested to determine whether human pathogens, including antimicrobial-resistant organisms, are present in orchards and whether antibiotic residues are potentially reaching the food supply.	Completed specimen collection; testing and data analysis in progress. Currently performing additional testing to determin antibiotic resistance in enterococci and other bacteria found in the collected specimens.
CDC	See Action Item #55 (Assessment of the off-farm transport of waste-associated chemical and microbial constituents present on swine feeding operations).	See Action Item #55 (Assessment of the off-farm transport of waste-associated chemical and microbial constituents present on swine feeding operations).	See Action Item #55 (Assessment of the off-farm transport o waste-associated chemical and microbial constituents present on swine feeding operations).
CDC	See Action Item #55 (Sampling for Antibiotics in agricultural river basin).	See Action Item #55 (Sampling for Antibiotics in agricultural river basin).	See Action Item #55 (Sampling for Antibiotics in agricultural river basin).
CDC	See Action Item #55 (Evaluation of the impact of flooding on water quality and human health indicators).	See Action Item #55 (Evaluation of the Impact of Flooding on Water Quality and Human Health Indicators).	See Action Item #55 (Evaluation of the Impact of Flooding on Water Quality and Human Health Indicators).
USDA	AR of enteric bacteria in poultry or food-producing animals	The project plan has three broad objectives: 1) determine the impact of antimicrobial use on the prevalence of drug-resistance in enteric bacteria; 2) elucidate mechanisms that contribute to the acquisition, dissemination, and persistence of antimicrobial resistance in food-borne pathogens; and 3) develop models to measure the frequency of emergence and transfer of AR.	Ongoing. Bischoff, et al, College Station, TX.
USDA	Sources and risk factors for Campylobacter in poultry and impact of human disease in a closed system (Iceland)	This study will look at 3 potential sources of Campylobacter and measure the risk factors for contamination of broiler flocks in a closed production system.	Ongoing. Stern, Lowman, Hiett, Athens, GA.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
USDA	Ecology of intermittent Salmonella infections in dairy milk shed	The goal is to determine the spatial and temporal attributes of the Salmonella by serotype and molecular types in dairy milk shed; compare on-farm attributes of herds; and determine intervention strategies	Ongoing. Sischo, University of California.
USDA	AR of foodborne pathogens linked to a multiple AR operon	This project will determine the impact of induction of E. coli O157:H7 and S. Enteritidis multiple antibiotic resistance (mar) locus on resistance to structurally unrelated compounds including antibiotics, sanitizers, and food preservatives.	Ongoing. Mathews, Rutgers University.
USDA	Plasmid Biology 2002 Symposium	The objectives of the Plasmid Biology 2002 Symposium were to bring together scientists working in all the areas of basic and applied plasmid biology to discuss the latest progress and advances in the field.	Ongoing. Khan, Sobecky, University of Pittsburgh.
USDA	Oxytetracycline resistant gram-negative bacteria in dairy cattle: risk factors and implications on food safety	The purpose of this study is to gather relevant and accurate information on the epidemiology (descriptive and molecular) of oxytetracycline resistant gram-negative bacteria in dairy cattle. This study will provide much needed scientific information with reference to prevalence, and on trends of antimicrobial resistance on the farm with respect to oxytetracycline and other antimicrobial agents. The investigators will also identify risk factors for resistance development and develop and implement interventions to reduce risk for resistance.	Ongoing.
USDA	Assessment of the pathogenicity of *Campylobacter jejuni* in broilers	University of Arizona researchers will determine the prevalence of the bacteria named *Campylobacter jejuni* in broiler chickens. This bacteria is a source of foodborne illness in humans. The grant will also be used to train processors to identify those broiler chickens that may have the bacteria.	Ongoing. Joens, University of Arizona.
USDA	Interventions for controlling AR of Salmonella and Campylobacter in dairy cattle	Michigan State University will develop methods to control microbes in dairy cattle from becoming resistant to the antibiotics that kill foodborne pathogens	Ongoing. Kaneene, Michigan State University.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
USDA	Source, diversity and resistance of foodborne pathogens in swine and pork	North Carolina State University researchers will investigate the source, diversity and resistance of two harmful bacteria (Salmonella campylobacter and Yersinia) in two sets of swine: one that has received antibiotics and one that is free of antibiotics. The investigation will help predict which group of swine will be more resistant to the pathogens and less expensive to own.	Ongoing. Gebreyes, North Carolina State University.
USDA	*Salmonella Newport* infections in dairy cattle: epidemiology and on-farm management	Pennsylvania State University researchers will investigate the extent of infection/contamination of *Salmonella Newport*, a newer microorganism, on farms and its effect on cattle. This data would lead to prevention/treatment programs.	Ongoing. Love, Pennsylvania State University.
USDA	The moral economy of antimicrobials in animal agriculture: advancing policy and practice in an era of AR	Texas A&M University researchers will identify optimum approaches for managing and regulating antimicrobial use while developing and delivering a curricula and educational materials on antimicrobial resistance for use by veterinarians and cattle producers.	Ongoing. Scott, Texas A&M University
Action Item #52: Develop Rapid Tests For Inspecting Fresh Commodities Like Fruit For Evidence Of Contamination With Bacteria That Are Resistant To Antibiotics.			
FDA	Rapid methods development	Develop rapid methods for the identification of foodborne pathogens in animal feed.	Extramural contract with University of Tennessee awarded.
Action Item #53: Evaluate the Effect of Current Food Processing and Distribution Methods on the Emergence and Spread of Drug-Resistant Organisms.			
Action Item #54: Identify and Evaluate New Food Pasteurization Strategies.			
Action Item #55: Assess the Risk of AR Emergence and Spread due to Environmental Contamination by Antimicrobial Drugs or by Resistant Bacteria in Animal and Human Waste. Collect Information on Whether Environmental Contamination by Antimicrobial Drugs Can Lead to the Development of Resistance in Bacteria That Live in Soil or Water.			
CDC	Assessments of the off-farm transport of waste-associated chemical and microbial constituents present on swine-feeding operations	Soil and water samples are being assessed in the vicinity of a large farm to determine whether selected chemical and microbial constituents found in swine manure are traveling from agricultural fields onto which swine manure is applied into the local environment.	Enzo R. Campagnolo, et. al. Antimicrobial residues in animal waste and water resources proximal to large-scale swine and poultry feeding operations. The Science of The Total Environment, Volume 299, Issues 1-3, Pages 89-95, November 2002.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CDC	Sampling for antibiotics in an agricultural river basin	Sample and analyze water and bed sediment from streams in an agricultural river basin (containing livestock and crop farms) for antibiotics, nitrogen, and microbes and their antimicrobial susceptibilities.	Completed specimen collection. Analysis pending.
CDC	Evaluation of the impact of flooding on water quality and human health indicators	Assess possible chemical and microbial contamination of surface and drinking well water in two counties that experienced flooding. This assessment includes (1) the exploration of the association between presence of concentrated animal feeding operations and levels of environmental contamination in surface, estuarine, and well water and (2) investigating the presence of human pathogens and their antimicrobial susceptibility as an indicator that may result from environmental contamination of surface and well water.	Specimen collection in progress. Analysis pending.
USDA	Enteric pathogens in oysters	This study will assess the relationship between fecal coliforms present in the water column and the prevalence of pathogens in oysters sold in retail markets. It will try to determine primary sources (human vs. agricultural) of fecal contamination,	Ongoing. Joens, University of Arizona.
Action Item #56: Assess the Impact of Antimicrobial Use in Companion Animals (Pets) on Colonization and Infection with Drug-Resistant Organisms in The Animals and Their Humans Household Contacts.			
Action Item #57: Work with Veterinary and Agricultural Communities To Help Educate Users of Veterinary and Agriculture Antimicrobials About AR Issues, and Promote the Implementation and Evaluation of Guidelines That Address These Issues.			
CDC, FDA, USDA	Liaison with American Veterinary Medical Association Steering Committee on Antimicrobial Resistance	Participate in committee activities, including development of prescribing principles and educational programs.	The committee developed General Principles for Judicious Therapeutic Use of Antimicrobial (1998), which were then adapted by species groups for their membership, to date including swine (1999), poultry (2000), bovine (2000), feline (2001), and equine (2001). Implementation is promoted through educational programs and a computerized veterinary decision support system, which is under development.
CDC	Development of model veterinary school curriculum to promote appropriate antimicrobial drug use	A curriculum is being developed in collaboration with partners that will be offered to veterinary schools.	Discussed content and structure with the American Veterinary Medical Association's Steering Committee on Antibiotic Resistance, representatives from bovine and swine veterinary organizations, and members of the academic veterinary community. Initiated development of Web-based course material with partners at Michigan State University, College of Veterinary Medicine.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
FDA	Education/outreach materials	Develop outreach material on judicious use targeted to veterinarians.	Ongoing activity. Contract awarded with the American Veterinary Medical Association to develop the guidelines. Guidelines received and from these, videotapes and brochures produced for veterinary practitioners. 1) Published four booklets that explain prudent use principles in depth for beef, dairy, swine and poultry veterinarians and sent the appropriate booklet to food animal practitioners. 2) Produced two videotapes to be used at meetings and veterinary medical schools to introduce the prudent drug use principles.
USDA/FDA	Education programs to producers	University based programs to educate producers on the difference between a.r. and residues.	Ongoing
**** TOP PRIORITY **** **Action Item #58: In Consultation with Stakeholders, Refine and Implement the Proposed FDA Framework for Approving New Antimicrobial Drugs for Use in Food-Animal Production and, When Appropriate, for Re-Evaluating Currently Approved Veterinary Antimicrobial Drugs.**			
FDA	Drug categorization	Develop an approach for how to evaluate drugs as to their importance in human medicine for use in animal drug premarket application requirements for use in CVM's guidance for industry on the strategy for ensuring the safety of new animal drugs with regard to their microbiological effects on bacteria of human health concern.	An approach for ranking antimicrobial drugs as to their importance for human medicine was developed by CDER and incorporated into CVM's draft guidance published in November 2002. Comments on the approach were obtained from the CDER Anti-infective Advisory Committee in January 2003. These comments are currently being considered in th development of a final guidance.
FDA	Fluoroquinolones	Withdraw approval of fluoroquinolones for use in poultry	Sarafloxacin voluntarily withdrawn April 30, 2001; hearing requested for Bayer's enrofloxacin. Legal proceedings ongoing. Both sides have filed narrative statements, written direct testimonies, and detailed proposed findings of fact. Oral cross examination scheduled between April 28 and May 9, 2003.
FDA	Risk assessment	Risk assessment: Conduct an analysis of the relationship between emergence of streptogramin-resistant *Enterococcus faecium* (Synercid) in humans and use of streptogramins (virginiamycin) in food-producing animals.	Draft risk assessment for distribution and public comment planned for 2003.
FDA	Pathogen load	Develop guidance relating to antimicrobial drug effects on pathogen load and incorporate into CVM's guidance for industry on the strategy for ensuring the safety of new anima drugs with regard to their microbiological effects on bacteria of human health concern.	Literature review published on CVM website May 2001. Veterinary Medicine Advisory Committee meeting held January 22-24, 2002. Based on the lack of scientific consensus on the issue, CVM has decided not to pursue guidance regarding pathogen load effects at this time.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
FDA	Microbiological safety requirements	Develop pre-approval requirements for microbiologic safety regarding the use of antimicrobial agents in food-producing animals. Incorporate into CVM's guidance for industry on the strategy for ensuring the safety of new animal drugs with regard to their microbiologic effects on bacteria of human health concern.	Draft guidance for industry was published in September 2002. Public meeting was held in October 2002 to present guidance document and obtain public comment. Comment period from the guidance closed in November 2002 and an analysis of comments received has been completed. Work i currently ongoing to revise draft guidance based on the comments received. Publication of the final guidance is expected by the end of 2003.
FDA	Antimicrobial use in food-producing animals	Develop rulemaking relating to annual reports of use and quantity of antimicrobial drugs marketed for food animals	Participated in WHO expert consultation on monitoring drug use in September 2001. Developed draft proposed rule and guidance. FDA is holding proposed rule and guidance while assessing economic impact of the proposed regulation.
FDA	Framework document	Refine the Framework Document and incorporate the concepts into guidance for industry on a strategy for assuring the safety of new animal drugs with regard to their microbiological effects on bacteria of human health concern.	Comments from public meetings and submitted to the Framework Document have been incorporated into guidance; small, outreach meetings held with stakeholder groups throughout 2001 for additional input. Key concepts from the Framework Document have been incorporated into the draft guidance for industry published in November 2002. Publication of a final guidance is expected by the end of 2003.
Action Item #59: Strongly Encourage Involvement of Veterinarians in Decisions Regarding the Use of Systemic Antimicrobial Drugs in Animals, Regardless of the Distribution System Through Which the Drug Is Obtained (e.g., Regardless of Whether a Prescription Is Required To Obtain the Drug).			
FDA	Educational materials	Develop outreach materials on judicious use targeted to food animal producers.	Based on the information developed for veterinarians, FDA developed and printed booklets for swine producers and poultry producers, written with less technical language. Have contracted with specialists to write booklets for dairy and bee producers. These booklets have been printed and distributed.
FDA	AR use by veterinarians	Develop a Web-based decision support system for use by veterinarians to select and use antimicrobial agents appropriately.	Provided funding for development of Veterinary Antimicrobial Decision Support System; five year contract awarded late 2001.
Action Item #60: Evaluate the Potential Impact of Making All Systemic Veterinary Antimicrobial Drugs Available by Prescription Only.			
Action Item #61: Convene an Expert Group To Consider How To Incorporate AR Issues into Regulations Governing the Registration and Use of Antimicrobials and Antibiotic Pesticides. Invite External Experts, Stakeholders, and the Public To Provide Input.			

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
Action Item #62: Establish an Ongoing Mechanism To Obtain Periodic Input from External Experts on AR Issues. This Process Will Include Ensuring Input from Stakeholders and Partners (e.g., State and Local Health Agencies, the Private Sector, and the Public) in Developing and Reviewing Federal Efforts To Address Antimicrobial Resistance.			
ARHQ, CDC, DoD, VA, EPA, FDA, NIH, USDA	Antibiotic resistance task force	Annual Progress Report and Public Meeting.	In 2002, progress report issued consisting of inventory of projects that address Action Plan items. Second annual public meeting June 25, 2003, Bethesda, MD. Convened consultants meeting to discuss issues relating to writing of Part II of the Action Plan (Global Issues), September 26, 2002, San Diego, CA. Sent Task Force Representative to World Health Organization to help WHO implement Global strategy on AR.
CDC	Board of Scientific Counselors, National Center for Infectious Diseases	Discussion of CDC activities to address AR at Board meetings, including extended discussion in breakout group in 2002.	Ongoing.
**** TOP PRIORITY **** **Action Item #63: Support Demonstration Projects To Evaluate Comprehensive Strategies That Use Multiple Interventions To Promote Appropriate Drug Use and Reduce Infection Rates.**			
CDC	Wisconsin Antibiotic Resistance Network (WARN)	The Wisconsin Antibiotic Resistance Network (WARN) is a statewide program to reduce antibiotic overuse and reduce the spread of resistant bacteria that cause upper respiratory illnesses. WARN is a partnership between the State Medical Society of Wisconsin, the Marshfield Medical Research Foundation, and the Wisconsin Division of Public Health. Recent activities include antimicrobial susceptibility testing; implementation and evaluation of educational interventions for the community, health departments, and health professionals; pharmacy outreach, and economic analyses to determine intervention costs.	Ongoing. Supported by CDC Cooperative Agreement throug 2003. 2002 progress included production of a parent and adult survey to assess knowledge, attitudes, and practices (KAP) regarding resistance, surveillance for drug-resistance *S. pneumoniae* infections through the Wisconsin Department of Health, analyses of prescribing trends/data from healthcare data, and an evaluation of the availability of WARN educational materials in pediatric and family practice clinics.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CDC	The Chicago Antimicrobial Resistance Program (CARP)	CARP is a 5-year demonstration program to determine the impact of antimicrobial use and infection control interventions on the reduction of antimicrobial resistance in a healthcare delivery system. Components include developing improved methodology for interhospital and intrahospital comparisons of AR rates, computer-based surveillance of antimicrobial drug use, and interventions to improve antimicrobial drug use and prevent emerging resistance. It is hoped that the project will demonstrate methods for adherence to hand hygiene, decreases in rates of MRSA and VRE, reductions in use of broad-spectrum antibiotics and antimicrobial regimens with redundant antimicrobial spectra, and model the costs of healthcare associated infections.	Ongoing. Supported by CDC Cooperative Agreement throug 2003. 2002 accomplishments include measured increases i adherence to hand hygiene practices, measured increases i compliance with guidelines for treating infections, decreases in inappropriate use of antimicrobials, and an overall decrease in MRSA. The first phase of a comprehensive cost study for AR was completed, and manuscripts detailing progress submitted for publication.
CDC	IMPART (Inter-Mountain Project on Antimicrobial Resistance and Therapy)	A project to implement and evaluate a comprehensive approach in rural Utah and Idaho communities (in both inpatient and outpatient settings) for surveillance of AR, to improve antimicrobial prescribing, to assess the environmental impact of antimicrobial drug use in agriculture and aquaculture and to evaluate potential routes of transmission of resistant bacteria to humans, and to identify novel biotherapeutic approaches to AR that have applicability to the rural setting.	Three year grant awarded in 2001. During the first year of this study a comprehensive surveillance system has been established to monitor AR and assess the impact of antimicrobial drug use in agriculture and aquaculture. Data collection is underway with preliminary results expected in 2003.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CDC	Comprehensive demonstration project: building regional coalitions to prevent methicillin-resistant *Staphylococcus aureus* (MRSA) in healthcare facilities	This project supports the development and implementation of comprehensive programs to reduce the incidence of MRSA infections in states and/or large regional networks acute phase and nonacute phase healthcare facilities. The Pittsburgh Regional Healthcare Initiative (PRHI) was recruited as a collaborating partner for this project. PRHI is a coalition of regional healthcare facilities and civic, corporate, and healthcare leaders in the Pittsburgh area dedicated to improving the quality of healthcare delivery in southwestern Pennsylvania. An intervention plan is being developed which involves applying a process engineering technique borrowed from the automotive industry Toyota Production System (TPS) to the processes of patient care that contribute to the problem of AR. The technique is designed to maximize the quality and efficiency of complex systems of work. Improving the design and flow of work should remove barriers to compliance with recommended prevention strategies.	Ongoing. Initiated pilot testing of the interventions in two hospitals within the network (University of Pittsburgh Medical Center-Presbyterian Hospital and Pittsburgh Veterans Administration Hospital) during 2001 baseline compliance with infection control practices such as hand hygiene was low. Follow-up observations show significant improvement in compliance across all occupations. Problems hindering compliance which continue to be targeted include unreliable delivery of isolation materials, inconsistent identification of patients requiring isolation, and time consuming inefficiencie in the delivery of patient care services such as medication administration. In addition, an assessment of policy, perception, and practice regarding MRSA control has been initiated.
VA	See Action Item #39.	See Action Item #39.	See Action Item #39
Action Item #64: Utilize Federal Health Care Systems (e.g., DoD, VA) as Models for AR Surveillance and Prevention and Control Activities Involving Appropriate Drug Use, Optimized Diagnostic Testing, Infection Control, and Vaccination Practice.			
VA	See Action Item #39.	See Action Item #39.	See Action Item #39.
Action Item #65: For All Healthcare Systems for Which Federal Funds Are Provided, Identify and Promote Strategies To Establish AR Prevention and Control Activities as Part of Quality Monitoring Programs.			
Action Item #66: Encourage Nationally Recognized Accrediting Agencies such as The National Committee for Quality Assurance (NCQA), and the Joint Commission on Accreditation Standards That Promote Efforts To Prevent and Control AR, Including Appropriate Use, Infection Control, Vaccine Use, and Diagnostic Testing. These Standards May Draw on the Findings of Existing Data and Demonstration Programs and AHRQ Evidence-Based Practice Centers.			

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
AHRQ	Ongoing development and evaluation of HEDIS measures.	Grant to Harvard University for a rigorous and broad evaluation of HEDIS 3.0 specifically: 1) evaluate the new "reporting set" measures in HEDIS 3.0 and a subset of the original "reporting set" measures with respect to their relevance for users, the soundness of the science that underlies them, and the feasibility of implementing them; 2) develop complete operational specifications for a subset of "testing set" measures that are particularly strong candidates for the next version of HEDIS; and 3) evaluate the "testing set" measures that might be used in the next version of HEDIS with respect to their relevance, scientific soundness and logistic feasibility.	Based on these analyses, refinement of specific measures will be suggested and important problems will be identified with individual indicators to guide decisions about whether to include these indicators in subsequent versions of HEDIS. This work is proposed as part of a general strategy and method for developing and refining measures such as HEDI in the future.
VA	Quality assurance programs	The Office of Quality and Performance's Performance Measurement Program, which supports the VHA Strategic Plan, serves as a vehicle for effecting change in a balanced fashion. The Performance Plan operationalizes the premise that better quality, access, and satisfaction are often more efficient. For example, improved rates of inexpensive pneumococcal vaccinations may result in decreased antibiot use. Immunization rates are assessed through a contract chart review system and are part of managers' performance standards, and, therefore, are used as part of the VHA qualit monitoring program. This is part of the VHA patient care culture. Excellent immunization rates in the VHA have resulted from this program.	Ongoing.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
Focus Area III: Research			
Action Item #67: Additional Research, Including High Risk and High Payoff Research in Nontraditional Fields, Is Needed.			
NIH, DoD	Biotechnology Engagement Program (BTEP)	The BTEP Program is an attempt by the U.S. government to engage former Soviet Union scientists that conducted biowarfare research to refocus on issues of mutual benefit. DMID program staff oversee a U.S. – Russian Collaborative TB research project initiated in 2001 with Professor A. Llyichev of Vector in Novosibirsk entitled, "Drug resistant tuberculosis in Western Siberia." Staff oversee, "Molecular epidemiology and antibiotic resistance of bacterial infections in Georgia" in collaboration with Lela Bakanidze of the National Center for Disease Control of Georgia.	Collaboration ongoing.
CDC	Grant Program for Applied Research on Antimicrobial Resistance: Microbiologic Mechanisms of Dissemination of AR Genes and Relationship to Antimicrobial Drug Use	Awards for projects to develop information necessary to prevent and control the emergence and spread of resistance in selected bacteria through better understanding the mechanisms through which resistance develops and spreads in field settings.	Three three year awards were made in 2001. Research areas included AR among *E. faecium* in animal and human populations and fluoroquinolone resistance among *E. coli* in healthcare settings.
CDC	Grant Program for Applied Research on Antimicrobial Resistance: Characterization of Strains of Communit Associated Methicillin-Resistant *Staphylococcus Aureus*	Awards will be made to applicants who assemble a network of partners who identify and access a defined population of persons within which there is community-associated MRSA disease and data sufficiently prevalent to allow appropriate analyses; who obtain strains of *S. aureus* causing disease in this population with appropriate epidemiologic and clinical data to make findings generalizable to similar populations from diverse geographic areas; and who characterize strains and/or the relationship between these strains using a variety of molecular and biochemical techniques.	Awards will be made in September 2003.
CDC	AR mechanisms of *S. pneumoniae* (Alaska)	Use of PCR methodologies to rapidly screen *S. pneumoniae* isolates for genetic determinants of resistance; monitoring th emergence, spread, persistence, and decline of multidrug-resistance organisms by molecular-based typing capabilities to include multilocus sequence typing (MLST).	Ongoing. In 2002, expanded surveillance methodologies to include the molecular typing techniques Pulse Field Gel Electrophoresis (PFGE) and Multi Locus Sequence Typing (MLST) which allow an enhanced understanding of the emergence and transfer of resistance genes among these Pneumococcal isolates. Began retrospectively screening previously collected multidrug resistant isolates using these molecular typing techniques.
FDA	Multi-drug resistant TB	Identified genetic mechanisms causing resistance in multi-drug resistant tuberculosis.	Ongoing.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
FDA	Role(s) of mutators in natural populations	Conduct research on genetic diversity within populations of bacterial pathogens; Determine if mutator subpopulations of *Salmonella enteritidis* promote antibiotic resistance; Investigate role of bacterial persistence in emergence of AR.	Ongoing.
FDA	Acquisition of antibiotic resistance in *Salmonella* Newport	Investigate acquisition of multi-drug resistance in *Salmonella* Newport; Determine how resistance patterns, sources of organisms, and PFGE profiles correlate with phylogenetic distribution.	Ongoing.
FDA	DNA microarray profiling of antibiotic resistance genes.	Develop DNA microarray techniques and DNA chips for characterizing antibiotic resistance genes for multiple bacterial pathogens.	Ongoing.
FDA	Antibiotic resistance in *vibrio*	Investigate emergence of AR in *Vibrio* species.	Ongoing.
FDA	Studies on the Mechanism of fluoroquinolone (FQ) resistance and molecular screening for resistance determinants in Campylobacter, E. coli, and Salmonella	Isolate and characterize FQ resistant Campylobacter, *E. coli* and Salmonella from chicken and turkey farms.	21 FQ resistant campylobacter were isolated from chicken liver samples and characterized by PCR-RFLP and Pulsed field gel electrophoresis (PFGE).Seventy-eight campylobacters were isolated from turkey litter samples and characterized for the presence of galE gene, PCR-RFLP and PFGE. Quinolone resistance determining regions (QRDR) from campylobacters and E. coli were PCR amplified and sequenced for the detection of silent mismatched mutations. The FQ resistant E. coil strains isolated from chicken and turkey litter were typed by ribotyping.
FDA	Fate and degradation of antimicrobials, oxytetracycline (OTC) and sulfadimethoxine-ormetoprim (Romet 30) from aquaculture environmental samples	To isolate and characterize OTC and Romet 30 resistant Aeromonas spp., Pseudomonas, Citrobacter and *E. coli.* From aquaculture and catfish tissues.	30 OTC resistant Aeromonas spp. have been isolated. Thes isolates have been characterized by PFGE. These investigations are still in progress.
FDA	Develop a microarray chip for the detection of multiple antibiotic resistance markers	Oligonucleotide probes to detect resistance markers for 17 different antibiotics would be embedded in microarray slides. These would be hybridized with in vitro-labeled cDNA of the resistant bacteria isolated from farm animals or clinical samples. The microchip would help FDA efficiently monitor and track resistant markers and make regulatory decisions. It would also aid physicians for choosing appropriate antibacterial therapy.	These investigations are in progress.
FDA	Elucidation of the mechanism of resistance development in anaerobic bacteria from human intestinal tract	Evaluation of the effect of fluoroquinolones on the resistance development in the bacteria from the human intestinal tract and analysis of the fluoroquinolone resistance mechanism in anaerobic bacteria from the human intestinal tract.	Similar to aerobic and facultative anaerobes, both multidrug resistant pump and mutation in gyrase and topoisomerase IV are implicated in FQ resistance.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
FDA	Biodegradation of fluoroquinolone antibiotics	The fungus Pestalotiopsis guepini metabolized the fluoroquinolone antimicrobial agent norfloxacin to 7 amino-1-ethyl-6-fluoro-4-oxo- 1,4 dihydroquinolone-3-carboxylic acid and three other metabolites during growth on rice hulls used as poultry litter, suggesting that fungi that grow on poultry litter may be able to metabolize residues of fluoroquinolone drugs. The intestinal bacterium Enterococcus durans degraded 1-phenylpiperazine to N-acetyl-1-phenylpiperazine, N-formylaminoethylaniline and 2-phenylaminoethanol, suggesting a potential role in the breakdown of other compounds, such as fluoroquinolone drugs, that contain a piperazinyl group.	Ongoing.
NIH	Innovative approaches for combating antimicrobial resistance	A new initiative to stimulate novel and innovative research, including high risk and high payoff studies in nontraditional fields, to acquire a better understanding of the factors affecting the development of resistant pathogens and spread of resistance genes, in order to direct actions to diagnose, control, and treat AR.	RFA-02-009, Receipt date for applications 10-10-02, 98 applications received, 18 funded in early 2003.
NIH	Exploratory/developmental grants: technology applications to NIAID-funded research	A new solicitation for exploratory/developmental (R21) grant applications that facilitate the use of innovative/emerging technologies to currently funded research projects related to the study of infectious diseases (bacterial, viral, fungal, and parasitic), diseases caused by category A agents of bioterrorism, HIV/AIDS, basic immunology, and immune mediated conditions. This R21 mechanism is designed to capitalize on scientific opportunities that would augment the value of the project and may not have been available at the time of submission of the parent grant.	New program announcement (PAS-02-031) released December 5, 2001. Application receipt date February 26, 2002.
NIH	Investigator-initiated small research grant award program announcement	The R03 award supports small research projects that can be carried out in a short period of time, with limited resources. This solicitation extends its use to unsolicited applications in addition to its use in individual Requests for Applications (RFA) and Program Announcements (PA). This is an important mechanism for attracting new investigators to a field of study and providing sufficient support to allow development of preliminary data that will enable successful long-term funding.	New Program Announcement (PA-02-038) released on December 12, 2001. To be replaced by PA-03-108.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Investigator initiated grants mechanisms (R01)	NIH funds a diverse portfolio of grants to study AR in major viral, bacterial, fungal, and parasitic pathogens. Projects include basic research into the disease-causing mechanisms of pathogens, host-pathogen interactions, and the molecular mechanisms responsible for drug resistance, as well as applied research to develop and evaluate new or improved products for disease diagnosis, intervention, and prevention.	Ongoing.
NIH	Small Business Innovation Research and Technology Transfer Grants Program (SBIR/TTGP)	The SBIR/STTR program is an omnibus solicitation established under federal law that seeks to use small business to stimulate technological innovation, increase the participation of small business in federal R&D, and to increase private sector commercialization of technology development through Federal R&D. The annual set-aside for agencies with extramural research budgets over $100M is 2.5%.	Ongoing solicitation.
NIH	Small Business Innovation Research Advanced Technology Grants Program	This Program Announcement, SBIR-AT-NIAID, invites grant applications for SBIR projects with award duration and amounts greater than those routinely allowed under the SBIR program. This program announcement replaces PAR-00-126 that appeared in the July 26, 2000 issue of the NIH Guide. This program announcement includes instructions for applications for funds in excess of $500,000 annual total cost and new contact listings for inquiries.	Release Date: February 13, 2001 PA NUMBER: PA-01-052 National Institute of Allergy and Infectious Diseases Application Receipt Dates: April 1, August 1, December 1, 2001; April 1, August 1, December 1, 2002; April 1, August 1, 2003; http://grants2.nih.gov/grants/guide/pa-files/PA-01-052.html
NIH	Food and Waterborne Diseases Integrated Research Network (FWDIRN), expansion of the Enteric Pathogens Research Unit	The FWDIRN will consist of eight units (two each for clinical studies, microbiology, immunology, and zoonosis research) plus a coordination and biostatistics unit. This expansion addresses a heightened awareness of the ease of spread of food/water borne pathogens via intentional distribution. This contract will 1) evaluate vaccines, therapeutics, and rapid detection methods; 2) integrate human mucosal immunity with clinical research; 3) increase research and product development activities; and 4) include the ecology and microbiology of food/waterborne zoonosis as well as drug-resistant pathogens.	RFP DMID-03-04 and DMID-03-28 (Coordinating and Biostatistics Center). Closing date 11-18-02, to be funded in 2003.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Biodefense and Emerging Infectious Diseases Research Opportunities	In response to growing concerns about the use of biological agents in acts of terrorism, NIAID has expanded its biodefense research program. The ultimate goal of that expansion is to develop effective diagnostics, vaccines and therapeutics to protect the public in the event of a biological attack or the sudden emergence of select rare or eradicated diseases.	Notice AI-02-023; (http://grants1.nih.gov/grants/guide/notice-files/NOT-AI-02-023.html) In 2003 converted to PA-03-080; http://grants1.nih.gov/grants/guide/pa-files/PA-03-080.html.
NIH	Impact of Microbial Interactions on Infectious Disease Request for Applications	The intent of this RFA is to invite applications from investigators that would develop new approaches/technology and novel mechanistic ideas to examine polymicrobial interactions and to think beyond the one disease-one pathogen concept. Projects should include studies aimed at understanding the interactions of pathogens with the normal flora as well as the interactions among pathogens themselves, and how commensal organisms can be used to prevent or treat infections.	RFA-02-008. The review of the more than 100 applications took place in November 2002, awards to be made in 2003.
NIH	Scientific Advance: Researchers identify a gene that allows bacteria to resist antibiotic treatment	For nearly 40 years, antibiotics called quinolones have been used to treat bacterial infections; in many cases they are the "last line of defense" against serious infection. Those antibiotics block key bacterial enzymes that untwist the microbe's DNA so it can copy itself. Unfortunately, bacteria are becoming increasingly resistant to quinolones by adoptin changes in DNA on the microbe's chromosome. Scientists recently showed that quinolone resistance could also be transferred between some bacteria using smaller pieces of DNA called plasmids that are not part of the chromosome. Researchers have now identified a gene on those plasmids that accomplishes that task. The gene, named qnr, encodes a protein that protects one of the bacterial "untwisting" enzymes from the effects of quinolone drugs. The discovery of that novel gene sheds new light on quinolone resistance and suggests possible targets for new drugs.	Tran JH and Jacoby GA: Mechanism of plasmid-mediated quinolone resistance. Proceedings of the National Academy of Sciences 99: 5638-5642, 2002. Award Data : R01AI43312; George A. Jacoby, Lahey Clinic, Burlington, Mass.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Scientific Advance: Two-component regulator of *Enterococcus faecalis* cytolysin responds to cell density cues	Enterococcus bacteria are the main cause of highly drug-resistant infections acquired in hospitals. Some of the most serious bacterial strains produce a toxin, called a cytolysin, that damages surrounding tissues. Little is known about how that toxin is regulated. University of Oklahoma researchers recently identified two genes that work together to shut down cytolysin production. The investigators then showed how toxin production is switched on once the cells reach a specifi density. The identification of this two-component regulatory system that can sense the number of surrounding cells suggests a previously unknown mechanism of Enterococcus virulence. Researchers can now look for new ways to block the infection by interfering with the regulatory pathway.	Haas W, Shepard BD and Gilmore MS: Two-component regulator of Enterococcus faecalis cytolysin responds to quorum-sensing autoinduction. Nature 415:84-87,2002. Award Data: R01 AI41108; Michael S. Gilmore, University of Oklahoma
NIH	Scientific Advance: Modulation of virulence within a genetic center in Enterococci is described. Enterococci are bacterial inhabitants of the human intestine	They can also cause highly antibiotic-resistant infections in the hospital environment when the patient is seriously ill, immunocompromised, and/or receiving extensive antimicrobial therapy. Dr. Gilmore and his colleagues compared several strains of enterococci and found that virulence determinants were clustered on a large piece of DNA called a pathogenicity island. Pathogenicity islands have not previously been found a genetic element previously unknown in this genus. It appears that the pathogenicity island allows the normally benign bacterium to modulate and enhance virulence. In addition, previously unidentified genes were found associated with the pathogenicity island that appear to be associated with disease causing behavior of this opportunistic pathogen. This work was made possible by the availability of genomic sequences and genetic manipulation techniques.	Shankar N, Baghdayan AS and Gilmore MS: Modulation of virulence within a pathogenicity island in vancomycin-resistant *Enterococcus faecalis*. Nature 417: 746-750, 2002. Award Data: R01 AI41108; Michael S. Gilmore, University of Oklahoma
NIH	Scientific Advance: Researchers visualize the shape of drug resistance	Researchers from the United States and Australia recently reported the three-dimensional structures of a bacterial drug-binding protein attached to six different drugs. The protein, QacR, plays a key role in allowing some bacteria to resist the effects of antibiotics. The study provides important insight into how QacR grabs onto select drugs and explains features that are likely shared among different drug-resistance proteins. By understanding more about the molecular basis of antibiotic resistance, researchers hope to learn new ways to block the process.	Schumacher MA, Miller MC, Grkovic S, Brown MH, Skurray RA, and Brennan RG. Structural Mechanisms of QacR Induction and Multidrug Recognition. Science 294:2158-2163, 2001. Award Data: R01 AI48593; Richard G. Brennan, Oregon Health and Science University

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
USDA	Poultry: A food animal model for following antimicrobial resistant *Enterococci*	There is continued concern about the use of antibiotics as growth promoting agents in food animals and the potential for development of AR in human pathogens. The long term goal of this study is to understand the processes involved in the development and spread of resistance in gram positive bacterial flora of poultry. This study will collect microflora samples from commercial poultry farms and processing/slaughter plants for one year. The farms will have one house using growth promoting antibiotics throughout the flocks' life and one house with no antibiotics used. Comparisons of drug resistance genes and plasmids will be made between poultry gram-positive commensals and human enterococci. The human samples will be obtained from NARMS.	Ongoing: University of Georgia; Department of Avian Medicine; College of Veterinary Medicine.
USDA	Prevalence, strain types and antibiotic resistance of *Campylobacter* in turkey grow-out farms	*Campylobacter* is a leading cause of human food-borne illness in the U.S. Transmission involved primarily poultry, although pork, beef, raw milk, and other sources have also been identified. Resistance to several antibiotics, including fluoroquinolones, commonly used for treatment of human infections, is increasing in *Campylobacter*. Extensive studies with broilers suggest that birds become colonized in the farm, usually without symptoms, and that meat becomes contaminated during slaughter and processing. This study will investigate the prevalence of *Campylobacter* in sixty turkey growout farms in Eastern North Carolina. It will evaluate the impact of distinct turkey husbandry practices in the grow-out turkey farms, and of antibiotic use for veterinary purposes, on *Campylobacter* prevalence, strain types, and AR profiles. The results from this study will provide a currently unavailable database on *Campylobacter* colonization, subtypes and AR in turkeys.	Ongoing: North Carolina State University; Department of Food Science Grant 2001-35212-108.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
USDA	Clonal dissemination of antimicrobial resistant *Campylobacter jejuni* and *Escherichia coli*	There is an increasing concern that AR in both pathogenic bacteria and in the normal flora present a risk to the public health, and reduction in the degree of AR is an important public health goal. The antibiotic resistant flora that appear after antibiotic exposure of cattle and other food animals may be 'new' antibiotic resistant strains originating on the farm, or may be pre-adapted strains that originated elsewhere and were transferred to the farm by animals, feed, water, wildlife, humans, or other mechanisms. The origin is important, since different origins require different control measures. For *Salmonella typhimurium*, wide dissemination of AR strains is the predominant process. This study will look at whether wide dissemination of antibiotic resistant strains is also important in *Campylobacter jejuni* and *E.coli* in the bovine intestine. In addition, this study will determine whether AR *E.coli* can be competitively displaced by non- antibiotic resistant strains.	Ongoing: Washington State University, Department of Veterinary Microbiology and Pathology.
USDA	AR in swine given 5 in-feed antibiotic regimens	This study is designed to measure the association between the use of five antimicrobial regimens in swine and the presence of AR in human food-borne pathogens isolated from pigs on farms in the Midwest and their caretakers.	Ongoing: Large Animal Clinical Sciences, Michigan State University.
USDA	Determinants of AR in *Escherichia coli* isolated from calves	The goals of this project are to describe the dynamics of antibiotic resistance in commensal *Escherichia coli* isolated from calves, link the patterns of resistance to management and environmental attributes, define the economics of antibiotic use, and develop educational modules to describe approaches that minimize the occurrence of AR bacteria.	Ongoing: William Sischo, PhD University of California, Vet Med Teaching and Research Center.
USDA	Antibiotic usage and risk factors for AR in pork production	This three year study is designed to determine an association between the use of antimicrobial agents in swine production and the presence of AR in human foodborne pathogens isolated from slaughter pigs.	Ongoing: Bo Norby, PhD Large Animal Clinical Sciences, Michigan State University.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
USDA	Antimicrobial drug use and the development of resistant Enteric bacteria in dairy cattle	The objectives of this study are to 1) Determine the effect of antimicrobial treatment on the development of resistance in bacteria present in dairy cattle, 2) Develop and apply prudent antimicrobial-use guidelines specific for dairy cattle, and 3) Disseminate these guidelines to dairy producers and their veterinarians. It is expected that scientifically based interventions will be obtained and disseminated for use by veterinarians and dairy producers to address important issue of public health concern which pose a threat to their future livelihood.	Ongoing: Thomas Wittum, PhD The Ohio State University
USDA	Factors affecting the emergence of quinolone-resistant *Campylobacter* in poultry	The main goal of this project is to use an integrated approach to study quinolone-resistant campylobacters in the poultry reservoir and to establish an education and extension program on AR.	Ongoing: Qijing Zhang, PhD Food Animal Health Research Program, The Ohio State University.
USDA	Determination of the relationships between antibiotic resistance and virulence in*Salmonella*	Bacterial strains were obtained from clinical cases of salmonellosis and ARS found that a small group of multiple antimicrobial resistant Salmonella are capable of secreting a cytotoxin. The results demonstrate that the hypervirulent abilities of multiple AR Salmonella could be due to an ability damage cells within a host.	Ongoing: USDA-ARS: Ames, IA - National Animal Disease Center (NAD).
USDA	Develop a fundamental understanding of the process of antimicrobial resistance in order to prevent the spread of unwanted resistant factors among the microorganisms that live normally in the gut of swine and cattle	ARS used continuous culture models of gut bacteria to determine the effect of the drug vancomycin on bacteria within the continuous culture model and within the gut of animals. Although ARS previously demonstrated that growth of certain vancomycin-resistant microorganisms was prevented in the model by the bacterial mixture, ARS found that a sub-therapeutic concentration of vancomycin in the growth media will allow these microorganisms to survive in the culture. This information will be used to determine antimicrobial dose and duration regimens that are therapeutically effective but limit the spread of antibiotic resistant bacteria, and will ultimately lead to more appropriate approaches to using antibiotics in food animal agriculture.	Ongoing: USDA-ARS: College Station, TX.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
USDA	Determination of the persistence of antimicrobial resistant pathogens in the environment	The persistence of AR bacteria following the cessation of use of a given antibiotic is a problem for the development of effective intervention strategies to combat antimicrobial resistance. In collaboration with the FDA Center for Veterinary Medicine, ARS examined the antimicrobial resistance patterns of disease causing strains of Escherichia coli from newborn pigs experiencing diarrhea. ARS found that 53% of the isolates were resistant to chloramphenicol, a broad spectrum antibiotic that has been banned for use in food animals in the United States since the mid 1980s. This information will help to determine the factors that govern the persistence of resistance genes once an antibiotic is no longer used in animal agriculture.	Ongoing: USDA-ARS College Station, TX.
USDA	Assessment of the effect of penta-resistant bacteria on virulence and/or colonization	ARS challenged broiler chicks on the day of hatch with either a sensitive or penta-resistant *Salmonella typhimurium* DT104 and determined that penta-resistant bacteria did not cause clinical illness in broiler chicks. However, ARS did observe a significant increase in the numbers of birds that were colonized in the penta-resistant group. In contrast to *in vitro* studies, these data indicate that acquisition of multiple resistance does affect colonization rates but may affect the numbers of bacteria that may reach the food chain.	Ongoing: USDA-ARS: Athens, GA.
USDA	Characterization of Salmonalla serotypes on their ability to cause disease in animals and to acquire and disseminate AR genes	We determined that Salmonella serotypes differ in their ability to persist within the host and environment and have determined that both integrons (mobile genetic elements) and plasmids, play a role in dissemination of resistance genes.	Ongoing.Russell Research Center
USDA	Characterization of 3rd generation cephalosporin resistant Salmonella from animal sources	We characterized the strains and resistance mechanisms of 3rd generation cephalosporin resistant Salmonella in the United states and found that the CMY-2 gene is the most common mechanism by which Salmonellas acquire this resistance in the US.	Ongoing.Russell Research Center

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
USDA	Characterization of erythromycin resistance in enterococci isolated from swine farms using different regimens of tylosin	The effect of tylosin use on erythromycin resistant enterococci isolated from farms was investigated. Results from the study suggested that although resistance was highe on a farm where tylosin was used as a growth promotant, a few resistant enterococci also persisted on a farm where no antimicrobials were being used. Isolates from farms were analyzed for antimicrobial resistance gene content as well as genetic determinants for dissemination of resistance.	Ongoing.Russell Research Center
USDA	Evaluation of prevalence and antimicrobial susceptibility of *E. coli* isolated from fruits and vegetables	In collaboration with scientists from USDA-AMS, we are evaluating the prevalence and antimicrobial susceptibility of generic *E. coli* isolated from fruits and vegetables collected from different regions of the US. This information will be useful for determining the effect of antimicrobials on *E. coli* isolated from these sources and the potential impact that these bacteria may have on consumer health.	Ongoing.Russell Research Center
USDA	Evaluate the effect of Ionophores on fecal shedding of pathogens	We examined the effects of three ionophores (monensin, laidlomycin propionate, and bambermycin) on *Escherichia coli* O157:H7 and Salmonella typhimurium in experimentally infected sheep. Ionophore treatment had no significant effect on fecal shedding of the pathogens, on occurrence of the pathogens in lumen contents, nor on antimicrobial susceptibilities of the recovered isolates. The results sugges that short-term feeding of ionophores would have little or no adverse effect on Salmonella and *E. coli* populations in the ruminant.	Ongoing.Southern Plains Agric. Research Center, College Station TX

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
USDA	Evaluate the effects of low level feeding of antibiotics on microbial diversity and inhibitory stringency	We used a defined mixed culture of chicken gastrointestinal microflora maintained in a continuous-flow chemostat as a model to study the effects of the antibiotic tylosin on microbial diversity and inhibitory stringency. The microbial diversity in cultures treated with sub-therapeutic concentrations of tylosin was reduced (from 29 initial organisms to 3 after treatment), and the treated cultures failed to exclude *E. coli* O157:H7 in vitro. These results suggest that the use of tylosin at low doses for growth promotion may eliminate some beneficial anaerobic bacteria that normally serve as a natural host defense against enteric infection. Further research in a live animal model is warranted to determine whether tylosin treatment increases susceptibility of chickens to colonization by enteric pathogens.	Ongoing.Southern Plains Agric. Research Center, College Station TX
Action Item #68: Conduct Further Government-Wide Assessments with External Input on the Scope and Composition of AR Research To Identify Research Opportunities.			
NIH	Antimicrobial strategies and cardiothoracic surgery working group	Collaboration between NIAID and NHLBI to bring scientific experts together to explore novel research and antimicrobial strategies such as vaccines and drugs for use in the prevention and treatment of infections following cardiac surgery, including complications relating to the development of AR. The group of outside experts will identify gaps and opportunities for additional research to be supported by joint Institute ventures.	Meeting held April 4-5, 2002 in Bethesda, MD., collaborative clinical trials and research initiatives under development.
Action Item #69: Work with the Appropriate Peer Review Structures To Ensure That the Requisite Expertise Is Applied to the Review Process To Facilitate Funding of Quality AR Research.			
NIH	Bacteriology and mycology study sections	Recommendations for additional scientific reviewers with expertise in AR be added to selected study sections.	Recommendations were made, and selected reviewers with expertise in AR were added to study sections.

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NIH	The Panel on Scientific Boundaries for Review has conducted a comprehensive examination of the organization and function of the review process that is carried out by the Center for Scientific Review (CSR) at NIH. The purpose of this evaluation is to position the CSR peer review system so that it fosters expanded research opportunities, as well as permits the review system to keep pace with the accelerating rate of change in the way that health-related research is performed. This examination is being carried out in two phases, with extensive involvement of the extramural research community. The Panel has proposed a set of Integrated Review Groups (clusters of scientifically related study sections, referred to as IRGs) and proposed guidelines for study sections.	The Infectious Diseases and Microbiology IRG review by the Expert Working Group was conducted from May – August 2001 and developed a proposed set of guidelines and shared interests for new study sections. The period for public comment on these guidelines has closed. One of the proposed study sections is Drug Discovery and Mechanisms of AR.	The final phase involves developing study section rosters an timelines for implementation. The revised Infectious Diseases and Microbiology IRG will accept applications for the first time in June 2004 and the newly constituted study sections will begin review of grant applications in October 2004.
**** TOP PRIORITY **** **Action Item #70: Provide To the Research Community Genomics and Other Powerful Technologies To Identify Targets in Critical Areas for the Development of New Rapid Diagnostics Methodologies, Novel Therapeutics, and Interventions To Prevent the Emergence and Spread of Resistant Pathogens. Examples Include Tools Such as Microbial Genome Sequences, Information on Comparative Genomics, DNA Chip Technology, Informatics, and Assistance in the Application and Use of These Tools.**			
NIH, USDA, FDA, EPA, FDA	Microbe project interagency working group	NIAID staff is participating in the Microbe Project Interagency Working Group, which developed a coordinated, interagency five year action plan on microbial genomics, including functional genomics and bioinformatics in 2001 .	In 2002, this working group has continued to coordinate genomic activities across federal agencies including those related to biodefense and has also focused on issues related to genomic data release and usage and genomic databases (http://www.ostp.gov/html/microbial/start.htm).
FDA	Genomics and Proteomics	Research in support of the use of genomics, proteomics and other powerful technologies to identify targets in critical areas for the development of new rapid diagnostic methodologies, novel therapeutics, and interventions to prevent the emergence and spread of resistant pathogens.	Established microarray group and CBER core program (for producing and reading oligonucleotide microarray chips). Initiated several research projects related to vaccine development, AR, pathogen identification and detection.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	The tuberculosis research materials and vaccine testing contract (Colorado State University)	Through this contract, NIAID provides TB research reagents to qualified investigators throughout the world, enabling them to work with consistent, high quality reagents prepared from the highly contagious and technically demanding TB causative pathogen. Starting in 2002, this contract calls for making reagents available for functional analysis of mycobacteria. Screening potential TB vaccine candidates in appropriate animal models is also conducted through this contract. A new screening assay using gamma knock out mice which are more susceptible to TB infection) has been developed and is showing promising results.	To date, screened 211 candidates or combinations under thi contract. Supplemental funding by NIAID for the contract will support increased vaccine testing and in 2003 make availab reagents for genomic analysis of TB. Information and reagent request forms are available at; http://www.cvmbs.colostate.edu/microbiology/tb/top.htm
NIH	NIAID pathogen functional genomics resource center (PFGRC)	Contract (N01AI15447) to support the expanded program on pathogen genomics of the NIAID, with the goal of accelerating research for the systematic understanding of the genomic information of microbial pathogens and invertebrate vectors. The center will provide tools, including relational databases, computational tools, microarrays, and proteomics reagents; and training to scientists and researchers on utilizing genomic information to understand the disease-causing characteristics of a variety of pathogens and invertebrate vectors of infectious diseases. This RFP (AI02-02) was issued in response to recommendations developed by the Blue Ribbon Panel convened by NIAID in May 1999.	With the resources provided to the PFGRC, three organisms have been selected for reagent development in year one (*S. aureus, S. pneumoniae, S. typhimurium*), four additional organisms were selected in year two (Chlamydia, TB, *N. gonorrhae, P. falciparum*), and a total of ten organisms will be supported by year three. For each pathogen a set of core resources will be developed including the type strain, genomic DNA, PCR primer pair sets, DNA glass slide microarrays, and full length entry clone sets; (http://pfgrc.tigr.org/)
NIH	Sequencing of whole pathogen genomes	NIAID has made significant investment in large-scale project to sequence the genomes of medically significant bacterial, fungal, and parasitic pathogens. In addition, NIAID collaborates with other funding agencies to sequence larger genomes of protozoan pathogens such as the organism that causes malaria. A listing of currently active pathogen genome sequencing projects is available at http://www.niaid.nih.gov/cgishl/genome/genome.cfm The availability of microbial and human DNA sequences will open up new opportunities and allow scientists to examine functional analysis of genes and proteins in whole genomes and cells, as well as the host immune response and an individuals' genetic susceptibility to pathogens.	NIAID supported approximately fifty large-scale sequencing projects in 2002 for microbial pathogens and invertebrate vectors with publication of the complete genome sequences of *Staphylococcus epidemidis, Yersinia pestis, Escherichia coli* (CFT073), and *Salmonella paratyphi* A, among others.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	NIAID pathogen genomics website (http://www.niaid.nih.gov/dmid/genomes/)	The updated NIAID genomics website serves as a focal point to disseminate to the scientific community current information about NIAID's microbial genomics research program and related activities, including information on funding opportunities, policies, application procedures, priorities for large-scale genome sequencing projects, press releases, an currently funded large-scale genome sequencing projects.	Currently available to the scientific community.
NIH	Sexually transmitted pathogen genomic resources	NIAID continues to provide support for databases of genomic and postgenomic information on sexually transmitted pathogens; http://www.stdgen.lanl.gov/	Currently available to the scientific community.
NIH	Bioengineering Consortium (BECON)	BECON is a trans-NIH committee composed of representatives from each of the NIH centers, institutes and divisions, including representatives from other federal agencies www.grants.nih.gov/grants/becon/becon.htm.In 2002, NIAID continued to participated in two BECON program announcements that support multidisciplinary research with a focus on bioengineering to develop knowledge and/or methods to prevent, detect, diagnose, or treat disease or to understand human health and behavior. These grants allow biomedical research scientists to partner with scientists from other disciplines, including physics, mathematics, chemistry, computer sciences, and engineering, to approach current complex biological problems.	In 2002, seven BRG applications were received and two wer funded, and seven BRP applications were received and one application was funded. In addition, NIAID participated in BECON sponsored program announcement focused on funding SBIR and STTR grants in the area of nanotechnology (PA00-018 and PA02-125). NIAID received and funded three SBIR nanotechnology applications.
NIH	Network on Antimicrobial Resistance in *Staphylococcus aureus* (NARSA) contract	The network includes approximately 73 registered users including basic researchers, clinical laboratories and infectious disease clinicians involved in staphylococcal AR research. NARSA supports electronic sharing of information a yearly investigator's meeting, and a case registry and repository of well-characterized staphylococcal isolates including the newly emerged vancomycin resistant *Staphylococcus aureus* isolates.	Expansion of the repository is underway to include a representative panel of clinical methicillin-resistant *Staphylococcus aureus* (MRSA) isolates from a variety of disease conditions, research isolates, genome sequenced isolates, virulence and toxin-producing strains, and a broader representation of drug-resistant strains. NARSA has also sponsored a staphylococcus annotation meeting in collaboration with the Insitute for Genomic Research (TIGR) and a community MRSA meeting in collaboration with CDC. Information concerning NARSA can be found at: www.narsa.net

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Pneumococcal reference and resource laboratory	NIAID continues to support a pneumococcal reference and resource laboratory through a contract awarded to the University of Rochester. Its purpose is to develop and standardize pneumococcal assays and reference reagents, measure and quantitate antipneumococcal antibody responses, develop new pneumococcal functional antibody assays, and disseminate antigens and reagents.	Ongoing.
NIH	Brochure on NIAID's microbial genomics research program	This brochure highlights recent accomplishments in the areas of genome sequencing of microbial pathogens and invertebrate vectors of infectious disease as well as related functional genomic activities.	Ongoing.
NIH	Research Center Grant, "Structural Organization and Proteomics of TB"	Under this award (P50GM62410), a global consortium consisting of 128 laboratories from 60 institutions in 12 countries are determining and analyzing the structures of ov 400 functionally relevant *M. tuberculosis* proteins.	Currently, the consortium has crystallized seventy proteins and solved twenty structures (models). The structural and functional information for the TB consortium is publicly available through Web-based databases (http://www.doe-mbi.ucla.edu/TB/).
NIH	Application of Exploratory/Developmental Technologies to NIAID-funded Research	Program announcement (PAS-02-160) that solicited R21 grant applications as supplements to ongoing/active NIAID grants. The goal was to facilitate the application of innovative/emerging technologies to currently funded research projects related to the study of infectious diseases, diseases caused by category A agents of bioterrorism, HIV/AIDS, basic immunology, and immune mediated conditions. The program was designed to allow funded investigators to capitalize on scientific opportunities that would augment the value of the project and might not have been available at the time of submission.	In 2002, 84 grant applications were received and 28 funded. NIAID has recently re-released this PA for 2003. http://grants2.nih.gov/grants/guide/pa-files/PAS-02-160.html
NIH	Infectious Etiology of Chronic Diseases: Novel approaches to pathogen detection request for applications	In 2001 RFA-01-004 was issued by NIAID with co-sponsorship by NIDDK, NCI and ORWH to solicit applications on the development of novel or improved technologies to identify and validate the role of pathogens in chronic diseases for which an infectious etiology is suspected. Areas of particular interest are studies using recent technological approaches in genomics, molecular biology, proteomics and computational biology	Applications were reviewed in Fall 2001 and sixteen were funded in 2002. http://grants.nih.gov/grants/guide/rfa-files/RFA-AI-01-004.html

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	In 2002 the NIAID, NHGRI and Wellcome Trust co-sponsored the Workshop on Model Organisms Databases	Representatives of major model organism databases (community databases dedicated to a single or multiple related species), funding agencies, and other interested scientists met to discuss current and future needs for databases. Strategies were developed to increase the quali and decrease the cost and startup time, of newly publicly funded databases.	It is anticipated that a meeting report will be posted on NHGRI website in early 2003.
NIH	Network for Large-Scale Sequencing of Microbial Genomes	This initiative will provide for the rapid and cost-efficient production of high-quality, microbial genome sequences. Genomes to be sequenced include microorganisms considered agents of bioterrorism (Category A, B, and C), related organisms, clinical isolates, closely related species, and invertebrate vectors of disease and microorganisms responsible for emerging and re-emerging infectious diseases. NIAID's Microbial Genome Sequencing Centers will have the capacity to respond to national needs and government agencies' priorities for genome sequencing, filling in sequence gaps and therefore providing genome sequencing data for multiple usages including forensic strain identification and identifying targets for drugs, vaccines and diagnostics.	RFP-NIH-NIAID-DMID-03-10, closed 2-18-03
NIH	Biodefense and Emerging Infections Research Resources Program	The NIAID Bioinformatic Resource Centers, a companion initiative to the Microbial Genome Sequencing Centers, will develop, populate, and maintain comprehensive, relational databases to collect, store, display, annotate, query, and analyze genomic, functional genomic, structural and related data for microorganisms responsible for emerging and re-emerging infectious diseases, including those considered agents of bioterrorism. Both single organism databases, as well as multi-organism databases, especially in the area of agents of bioterrorism, will be sought.	RFP-NIH-NIAID-DMID-03-34, CLOSED 3-20-03
NIH	Biodefense Proteomics Research Programs: Identifying Targets for Therapeutic Interventions Using Proteomic Technology	NIAID Proteomic Centers are intended to develop and enhance innovative proteomic technologies and methodologies and apply them to the understanding of the pathogen and/or host cell proteome for the discovery and identification of novel targets for the next generation of drugs, vaccines, diagnostics and immunotherapeutics against microorganisms considered agents of bioterrorism.	RFP-NIH-NIAID-DMID-BAA-03-38 (and 03-45 Administrative Researches for Biodefense Proteomic Centers), close 5-15-03

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
USDA	Identification and detection of AR genes in intestinal bacteria	ARS developed PCR assays to differentiate among nine classes of tetracycline resistance genes (classes A, B, C, D, E, G, H, K, L) and the assays were validated by using known stock cultures. Three methods for extracting DNA from swine fecal samples were compared and a MoBio commerci kit chosen based on quantity and quality of DNA product. Culture methods for isolating tetracycline resistant bacteria from the swine intestinal tract were developed and used to analyze cecal bacteria from grower stage swine from a farm that has not used antibiotics for growth promotion purposes for at least three years. These methods will be useful to researchers and regulators for measuring antibiotic resistance and developing intervention strategies.	Ongoing: USDA-ARS: Ames, IA - National Animal Disease Center.
Action Item #71: Encourage Sharing of AR Data Between Industry and the Research Community, Including Genomics and Other Technologies.			
NIH/DoD	Collaboration on genomics technologies and resources	NIAID continued its agreement with the Defense Advanced Research Project Agency (DARPA) in support of genomics efforts targeted at pathogens of potential bioterrorist threat.	Through this collaboration with DARPA large-scale genome sequencing projects for *Brucella suis* and *Coxiella burneti* have been completed. Ongoing.
FDA	See Action Item #30: (Anti-Infective Drugs Adivsory Committee)	See Action Item #30: (Anti-Infective Drugs Adivsory Committee)	See Action Item #30: (Anti-Infective Drugs Adivsory Committee)
FDA	See Action Item #30: (Anti-Infective Drugs Adivsory Committee)	See Action Item #30: (Anti-Infective Drugs Adivsory Committee)	See Action Item #30: (Anti-Infective Drugs Adivsory Committee)
NIH	Wyeth Ayerst *S. aureus* transcriptional profiling data	Wyeth Ayerst *S. aureus* transcriptional profiling data have been made available to the Network on Antimicrobial Resistance (NARSA) in *Staphylococcus aureus* program for use by the scientific community through a link on the NARSA website. Information concerning virulence gene regulation generated from these studies will allow pursuit of new drug and vaccine targets.	Collaborations with NARSA investigators are ongoing.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Respiratory Pathogens Reference Laboratory Support Request for Proposals	NIAID will be recompeting and expanding a pneumococcal reference and resource laboratory through RFP DMID 03-37, entitled "Respiratory Pathogens Reference Laboratory Support". Since the reference laboratory will support the infection prevention program of the Respiratory Diseases Branch, DMID, NIAID, it will have the potential to serve as a reference laboratory for GBS and GAS as well as pneumococci and other bacterial pathogens. The focus of the laboratory will be development and standardization of assays and reference reagents, measurement of bacterial antibody responses and distribution of reagents.	Awards will be made in 2003.
Action Item #72: Bring New Researchers into the Field, by Utilizing Appropriate Strategies such as Training and Research Opportunities.			
VA	Proposal Regarding Antibiotic Resistance Fellowship	The Infectious Diseases Program Office proposed the initiation of a two-year VA Special Fellowship in the area of antibiotic resistance at six sites. The proposal required trainees to have completed internal medicine and infectious diseases speciialty and subspecialty residency training, and would have required scientific emphasis on antibiotic resistance.	The proposal was rewritten and restructured to focus on training leaders in Terrorism Response for the Future with emphasis on antibiotic resistance. A portion of the training was to include biologic threat agents (including pandemic influenza).
NIH	Research Scholar Development Award (RSDA)(K22)	The RSDA will provide support for postdoctoral fellows who are moving to assistant professor positions in an academic institution. The purpose of the RSDA is to ease the transition to an academic position by enabling the recipient to focus on the establishment of his/her research laboratory prior to submitting applications for grant support. This is intended to establish new young investigators in needed fields, including AR.	New initiative (PAR-02-018) released November 15, 2001.
NIH	Other ongoing training and research fellowship awards	PA-00-003 Mentored Clinical Scientist Development Award (K08) PA-00-004 Mentored Patient Oriented Research Career Development Award (K23) PA-00-005 Mid-career Investigator Award in Patient Oriented Research (K24)	Important ongoing programs are fostering the development of young scientists and clinical investigators.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	NIH Exploratory/Developmental Research Grant Award (R21) (R21)	This announcement redefines the National Institutes of Health (NIH) Exploratory/Developmental Research Grant Award (R21) mechanism, and extends its use as an investigator-initiated mechanism to a variety of Institutes and Centers (ICs) listed in the announcement. The R21 is intended to encourage exploratory and developmental research projects by providing support for the early and conceptual stages of these projects.	RELEASE DATE: April 18, 2003 PA NUMBER: PA-03-107 http://grants1.nih.gov/grants/guide/pa-files/PA-03-107.html
NIH	NIH Small Research Grant Award (R03)	This announcement redefines the National Institutes of Health (NIH) Small Grant (R03) mechanism, and extends its use to investigator-initiated applications at the Institutes and Centers (ICs) listed in the announcement. The R03 award supports small research projects that can be carried out in a short period of time with limited resources.	RELEASE DATE: April 18, 2003 PA NUMBER: PA-03-108 EXPIRATION DATE: April 18, 2006, unless reissued. http://grants1.nih.gov/grants/guide/pa-files/PA-03-108.html
Action Item #73: Organize Conferences That Address Research Issues Relating to AR.			
CDC, EPA, FDA, NIH, USDA	2003 National Foundation for Infectious Diseases Conference on Antimicrobial Resistance: Science, Prevention, Control	Scientific conference June 23-25, 2003 in Bethesda, MD, sponsored by National Foundation for Infectious Diseases, in collaboration with CDC, EPA, FDA, NIH, USDA.	Organized conference.
CDC, EPA, FDA, NIH, USDA	2002 National Foundation for Infectious Diseases Conference on Antimicrobial Resistance: Science, Prevention, Control	Scientific conference June 26-28, 2002 in Bethesda, MD, sponsored by National Foundation for Infectious Diseases, in collaboration with CDC, EPA, FDA, NIH, USDA.	Organized conference. Well attended international conference occurred on June 26-28, 2002, in Bethesda.
FDA, CDC, NIH	See Action Item #30 (FDA/IDSA/PhRMA Co-Sponsored Public Workshop)	See Action Item #30 (FDA/IDSA/PhRMA Co-Sponsored Public Workshop)	See Action Item #30 (FDA/IDSA/PhRMA Co-Sponsored Public Workshop)

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH/CDC	Workshop on Tuberculosis in Children	Co-sponsored together with IUATLD, WHO, CDC, IPA, NICHD this workshop which gathered a group of scientists and clinicians with expertise in childhood tuberculosis to review the current state of the science including resistance trends, to identify research and knowledge gaps and to develop a list of research priorities for pediatric TB.	October 6-7, 2002 in Montreal, Canada. Meeting summary under development.
AHRQ	Workshop on economics of antibiotic resistance	Conference organized by Resources for the Future at Airlie House, Virginia, April 5, 2001.	Conference proceedings published.
AHRQ	Expert Meeting—The use of oral antimicrobial agents in children: remaining questions	Conference sponsored by AHRQ on treatment of otitis media in children held April 20, 2002.	Bauchner H, Besser RE: Promoting the appropriate use of oral antibiotics: there is some very good news. Pediatrics 2003;111: 668-70.
NIH	Antimicrobial strategies and cardiothoracic surgery working group	Collaboration between NIAID and NHLBI to bring scientific experts together to explore novel research and antimicrobial strategies such as vaccines and drugs for use in the prevention and treatment of infections following cardiac surgery including complications relating to the development o AR. The group of outside experts will identify gaps and opportunities for additional research to be supported by joint Institute ventures.	Meeting held April 4-5, 2002, in Bethesda, MD.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	4th World Congress on Tuberculosis	NIAID served as Secretariat and co-sponsor of this meeting, which evaluated the state of the global TB epidemic since the last TB World Congress in 1992 with oral and poster presentations of topics in laboratory research, epidemiology, translational research, resistance trends, health policy, systems and services research. Approximately, 796 participants from 58 countries attended the World Congress. The meeting co-sponsors, donors and organizers included the: American Lung Association, American Thoracic Society, Bill & Melinda Gates Foundation, Coalition for TB R&D, Global Alliance for TB Drug Development, Infectious Diseases Society of America, International Union against Tuberculosis and Lung Disease, Open Society Institute, Pittsfield Anti-TB Association, Sequella Global TB Foundation, US Agency for International Development, CDC, FDA, NIH/ NIAID, and Fogarty International Center, The Rockefeller Foundation, The Royal Netherlands TB Association, The World Bank/WHO Special Programme for Research and Training in Tropical Diseases, The Wellcome Trust, and WHO/STOP TB.	Meeting held June 3-5, 2002 in Washington, DC.
NIH	DMID Program staff serve as external consultants or liaison to a variety of national and international TB-related groups	Program staff consult and serve as liaison members to national groups, including the Advisory Council for the Elimination of Tuberculosis (ACET) and the CDC TB Clinical Trials Consortium. International activities include chairing WHO's TB Vaccine Initiative Advisory Committee (TBVIAC), STOP TB Coordinating Board, and Chair of the STOP TB Vaccine Working Group. Program staff also serve as an external advisor to an EC-supported TB Vaccine Development Cluster that is coordinated by Dr. Brigitte Gicquel of the Pasteur Institute, France.	Ongoing.
NIH	A joint meeting of the U.S.-Japan Cooperative Medical Sciences Program, TB and Leprosy Panel	A joint meeting was convened by program staff in New Orleans, LA, July 15-17, 2001, to foster an exchange of idea and stimulate international collaborations between U.S. and Japanese TB and leprosy investigators. For more information about this program: http://www.niaid.nih.gov/dmid/other/usjapan/DEFAULT.htm	Ongoing.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
USDA	Meeting: Impact of antimicrobials on agriculture	USDA (Cooperative State Research, Education and Extension Service; Agricultural Research Service; and Food Safety and Inspection Service) financially supported a research colloquium sponsored by the American Society of Microbiology on the impact of antimicrobials in agriculture in November 2001. This meeting of 35-40 experts provided a forum to discuss the current status, future directions and actions related to the use of antimicrobial resistance in agriculture. The report will be released in Spring/Summer 2002.	Meeting held November 2001. Colloquium report released October 2002 with over 12,000 copies disseminated in 6 months. Obtain from ASM website.
USDA	Workshop: A workshop on epidemiologic methods and approaches for food safety	A USDA-CSREES (Cooperative State Research, Education and Extension Service) sponsored workshop, A Workshop on Epidemiologic Methods and Approaches for Food Safety - Fall 2000, included a section on antimicrobial resistance and how to improve methods and approaches to study it.	Meeting held Fall 2001. The proceedings can be obtained from the following website: http:\\www.unl.edu\ianr\vbs\wills\Epiconf
USDA	Forum on emerging infections, IOM, NAS	Participated in IOM meeting, The resistance phenomenon in microbes and infectious disease vectors - Implications for human health and strategies for containment. Proceedings (www.nap.edu).	Complete.
USDA	AR and impact on agriculture	Roundtable presentation at ASM annual meeting, May 2002. Salt Lake City, UT. Provided overview of ASM research colloquium on impact of antimicrobials in agriculture.	Complete.
Action Item #74: Explore the Need To Encourage Preclinical Studies on the Toxicology, Pharmacokinetics of Novel Therapeutic Agents for the Treatment of Multidrug-Resistant Pathogens And Facilitate the Transition of Potential Products from Preclinical to Clinical Studies Leading to Development by Industry of Novel Therapeutic Agents.			

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Pharmacokinetics & Pharmacodynamics of Antimicrobials in Animal Models Request for Proposals	The purpose of this contract is to stimulate research towards discovery of improved therapies for TB. The emergence of multidrug resistant tuberculosis has produced sizable medical challenges to the treatment and containment of infectious tuberculosis in the face of limited chemotherapeuti options. In order to facilitate the development of improved drugs for the treatment of TB, and particularly multidrug resistant TB, the NIAID requires the directed evaluation of selected novel synthetic and pure natural product compounds. This contract will provide critical support for investigator-initiated drug discovery, stimulate private sector sponsorship of new drugs, perform comparison (or confirmatory) studies from different sponsors, and provide information for selection of antimicrobial drug candidates for design of clinical studies. It will serve as the central facility for evaluation of novel compounds for physical, pharmacokinetic, and pharmacodynamic properties.	RFP-03-21. http://www.niaid.nih.gov/contract/archive/RFP0321.pdf
NIH	Basic and Clinical Approaches to Controlling Human Respiratory Pathogens Request for Proposals	NIAID will be recompeting the Respiratory Pathogen Research Units (RPRU) through RFP DMID 03-05, entitled "Basic and Clinical Approaches to Controlling Human Respiratory Pathogens". The RPRUs will form the basis of a coordinated, interactive, multi-disciplinary network to help support preclinical and clinical studies against selected human respiratory pathogens which include pneumococci, Group A Streptococci and Group B Streptococci. The focus will be the conduct of pre-clinical research activities that are designed to validate or lead to clinical studies and related clinical trials of candidate vaccines and therapeutics.	Awards will be made in 2003.
NIH	Workshop on Improved Methods for the Preclinical Evaluation of Antimicrobials for Tuberculosis.	Meeting sponsored by TBRU and The Sequella Global TB Foundation. The meeting discussed tools used to develop preclinical data for the support of clinical trials for new drugs and treatment protocols for tuberculosis, including the utility of pharmacodynamic evaluations.	Held May 23-24, 2002.
**** TOP PRIORITY **** **Action Item #75: In Consultation with Academia and the Private Sector, Identify and Conduct Human Clinical Studies Addressing AR Issues of Public Health Significance That Are Unlikely To Be Studied in the Private Sector.**			
FDA, CDC, NIH	See Action Item #30 (FDA/IDSA/PhRMA Co-Sponsored Public Workshop)	See Action Item #30 (FDA/IDSA/PhRMA Co-Sponsored Public Workshop)	See Action Item #30 (FDA/IDSA/PhRMA Co-Sponsored Public Workshop)

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH, NIAID	Division of AIDS Clinical Trials	Numerous trials underway: R. Semba, Johns Hopkins University, “Adjunct Vitamin Therapy for Tuberculosis and HIV/AIDS in Malawi.” F. von Reyn, Dartmouth-Hitchcock Medical Center, “Disseminated Tuberculosis in HIV infection: Epidemiology and Prevention” in Tanzania. C. Whalen, Case Western Reserve University, “Impact of Tuberculosis on HIV Infections in Uganda – Adjunctive Prednisolone Therapy.” R. Chaisson, Johns Hopkins University, “Novel TB Prevention Regimens for HIV-Infected Adults” in South Africa. R. Oberhelman, Tulane University, “Practical Diagnostics for AIDS-Related Pediatric TB, Peru”. C. Whalen, Case Western Reserve, “Randomized, Phase II Study of Punctuated Antiretroviral Therapy for HIV Infected Patients with Active Pulmonary Tuberculosis and CD4 count > 350 cells/mm3.” T Sok, Cambodian Health Committee, “A Cambodian Clinical Research Network for HIV/TB” – an exploratory, developmental grant. S. Abdool Karim, University of Natal, South Africa “Collaborative AIDS Programme of Research in South Africa.	Ongoing.
VA	VA research update	VA investigators have a rather extensive portfolio in antibiotic resistance research that for fiscal year 2000 identifies twenty-three separate funded proposals in AR. For 2001, there are twenty-nine funded projects related to AR by VA investigators. These funded research grants cover a wide spectrum of AR issues. In addition, these do not include large clinical trials that may have impact on AR such as collaboration with the NIH-funded HIV ACTG’s and pharmaceutical corporate-related research that is widespread throughout the VHA. A specific area of emphasis is transmission of resistance among organisms and spread of these organisms from person to person. Such topics as spread of resistance in nursing homes, the relationship of resistance to staffing levels, and work practices (organization as they relate to antibiotic resistance are all part of VA investigators’ portfolios and are topics unlikely to be studied the private sector. VA investigators continue to have an extensive and expanding portfolio in antimicrobial resistance research.	Ongoing. In 2001, twenty-eight projects related to bacterial resistance were underway, an increase of over 300% from 1997. Ongoing. In 2002, VA provided an increase in fundin for projects related to AR of approximately 62% when compared to 2001. The number of studies receiving VA-funded financing increased by 80% when comparing 2002 to 2001.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Tuberculosis Research Unit (TBRU)	The TBRU contract (N01-AI-95383) Case Western Reserve University continues to make progress in developing surrogate markers of disease and human protective immunity and in conducting clinical trials of potential new TB therapeutic, preventive, and diagnostic strategies. Well-characterized clinical samples will be available for distribution to qualified investigators worldwide through a newly established repository. Activities of the TBRU are coordinated with other major organizations involved in TB research, including CDC, USAID, FDA, WHO, the Global Alliance for TB Drug Development, and interested industrial partners.	On-going TBRU supported studies: Phase III study of short duration standard course chemotherapy (Uganda) Phase II study of rhIL-2 (Proleukin®) in HIV-noninfected Adults with Pulmonary TB (Uganda) Pilot immunologic and Microbiologic Predictors of Response to Standard Anti-TB Treatment (Brazil). http://www.tbresearchunit.org/
NIH	Bacteriology and Mycology Study Group (BAMSG)	A clinical studies collaborative group with the expertise to plan, design, construct, and conduct clinical studies addressing diagnosis, treatment, and prevention of serious fungal and healthcare-associated resistant bacterial infections. One component will focus on clinical strategies to decrease the frequency of nosocomial bacterial infections, reduce emergence of antimicrobial-resistant pathogens, and rapidly detect infection and resistance in the ICU setting. A reserve fund for orphan studies will enable the conduct of innovative and public health-oriented clinical studies independent of industry funding and support. An external consultative group reviews the scientific agenda and study concepts. An investigator meeting was held on August 28-29, 2002.	One protocol is under development for the healthcare-associated resistant bacterial infections component: "Infection control strategies to reduce colonization and infection caused by antimicrobial-resistant bacteria in adult and pediatric intensive care units," with the objective of determining the effectiveness of hand hygiene vs. combined infection control strategies, including screening and barrier precautions on incidence of colonization with resistant bacteria. Another investigator's meeting is scheduled for September 3 and 4, 2003 in Bethesda, MD.
NIH	Bacteriology and Mycology Biostatistical and Operations Unit (BAMBU)	This contract supports study planning, protocol design, development, implementation, training, safety monitoring, da management and analysis, site monitoring, manuscript preparation, and other necessary and regulatory activities of clinical trials conducted through the BAMSG (see item above contract.	Ongoing.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Vaccine and Treatment Evaluation Units (VTEUs)	The VTEUs are a network of university research hospitals across the United States that conduct Phase I, II, and III clinical trials to test and evaluate vaccine candidates for infectious diseases. Through these sites, researchers can quickly carry out safety and efficacy studies of promising vaccines in children, adult, and specific high-risk populations. The results of these trials may have a profound effect on public health here and abroad. Through numerous studies at the VTEUs, researchers have tested and advanced vaccines for malaria, tuberculosis, pneumonia, cholera, and whooping cough. In the last 6 years alone, NIAID has supported more than 110 clinical trials through the VTEUs.	Seven VTEUs were awarded in June 2002: Baylor College of Medicine, Cincinnati University Children's Hospital Medical Center, UCLA Center for Vaccine Research, St. Louis University Health Sciences Center, University of Maryland School of Medicine; University of Rochester School of Medicine and Dentistry, and Vanderbilt University Medical Center. VTEUs will conduct clinical trial work on two new anti-TB vaccines in partnership with Corixa Corp. (fusion protein vaccine) and UCLA/Sequella Global TB Foundation (recombinant BCG vaccine). Both candidate vaccines were originally developed with NIAID grant support. http://www.niaid.nih.gov/factsheets/vteu.htm.
NIH	Prevention of group B streptococcal (GBS) disease contract	The RFP solicits proposals for the recompetition of a collaborative multidisciplinary five-year research effort focused on prevention of group B streptococcal (GBS) infection and disease. In this proposed new award, the major focuses will be on clinical studies in selected populations to further understand the nature of GBS infection, and on studies of the host immune response to GBS.	http://www.niaid.nih.gov/contract/archive/RFP0213.pdf. Brigham and Women's Hospital was awarded contract N01-AI-25495 in 2002.
**** TOP PRIORITY **** **Action Item #76: Identify, Develop, Test, and Evaluate New Rapid Diagnostic Methods for Human and Veterinary Uses with Partners, Including Academia and the Private Sector. Such methods Should Be Accurate, Affordable, and Easily Implemented in Routine Clinical Settings.**			
CDC	*C. trachomatis* resistance	*Chlamydia trachomatis* causes a sexually transmitted infection in an estimated 3 million Americans annually; untreated women can develop pelvic inflammatory disease, which can lead to chronic pelvic pain, infertility, and potential fatal ectopic pregnancy. Several methodologies are used to assess antimicrobial susceptibility among *C. trachomatis* isolates, and this project will compare those that are currently used in an attempt to develop a standardized/reproducible assay that can be utilized for monitoring treatment efficacy.	Preparing a report on a meeting of external consultants (which took place prior to 2002) and are organizing an international meeting to be held in conjunction with International Society for Sexually Transmitted Diseases Research (ISSTDR) on July 30, 2003 to share our preliminary meeting report and dialogue about further proble solving.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
DoD	Evaluation of commercial rapid diagnostic tests for influenza	Military populations are prone to outbreaks of febrile respiratory disease. It is expected that the use of rapid diagnostic tests for determining influenza as the cause of these outbreaks will aid in reducing unnecessary antimicrobial usage and hence help slow the emergence of AR in respiratory pathogens of bacterial origin. Two rapid diagnostic tests were evaluated against viral cultures betwee 1999 and 2001. Results showed a respective sensitivity and specificity of 100% and 63% for one test and 61% and 93% for the other. One of the evaluated rapid tests may be useful in respiratory disease outbreaks, but was not considered suitable for diagnoses in individual patients.	Study completed. Provided individual and summary results the military treatment facilities providing specimens and presented them at a national meeting.
FDA	Test kit evaluation	Work to develop streamlined mechanisms for evaluating rap diagnostic test kits for identifying microbes and for determining susceptibility to treatments. Work with academia and industry to produce guidance documents and reference methods that could be used in evaluating new rapid diagnostics for use in the clinical setting.	1) CDRH approved a whole blood IFN-gamma assay as an aid in detection M. tuberculosis infection. CDC funded studies to support clinical performance of the assay in a collaborative effort with the manufacturer. Walter Reed Army Institute also provided resources for additional evaluations. 2) Completed classification for devices intended to determine resistance and susceptibility to bacterial pathogens in a shortened incubation time period. Classification Regulation published May 8, 2000. 3) On February 5, 2003 CDRH published the special control guidance document for antimicrobial susceptibility test systems. This will provide to industry the necessary elements for data gathering and presentation.
FDA	Rapid diagnostic methods to detect multi drug resistant TB (MDRTB) strains	Research: development of rapid diagnostic methods for detecting MDRTB based on the microarray technology.	Collaboration of CDRH with CBER.
FDA	New rapid diagnostic methods	Research: new rapid diagnostic methods for bacterial contamination of foods.	Collaborating with CFSAN research. Developed new detection method using antibodies attached to chip. Working to establish limits of detection and apply to variety of foodborne agents.
FDA	Surveillance activities	Coordinate surveillance activities with CDC.	Held initial meeting with CDC April 25, 2001; further discussions ongoing.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
FDA	Nucleic Acid Tests (NAT) for detection of bacteria in donated blood products	Research: Development of nucleic acid tests (NAT) based on PCR-test, TaqMan assay and DNA microarray to detect transfusion induced sepsis causing gram positive and gram negative bacteria potentially present in donated blood products. This technology can be easily adapted to detect bloodborne antibiotic resistant bacteria.	Ongoing project: Awarded Director's Targeted Research Grant, CBER, FDA.
NIH	Biodefense and Emerging Infectious Diseases Research Opportunities	In response to growing concerns about the use of biological agents in acts of terrorism, NIAID has expanded its biodefense research program. The Ultimate goal of that expansion is to develop effective diagnostics, vaccines and therapeutics to protect the public in the event of a biological attack or the sudden emergence of select rare or eradicated diseases.	Notice AI-02-023; http://grants1.nih.gov/grants/guide/notice-files/NOT-AI-02-023.html. In 2003 converted to PA-03-080; http://grants1.nih.gov/grants/guide/pa-files/PA-03-080.html.
NIH	Biodefense Partnerships: Vaccines, Adjuvants, Therapeutics, Diagnostics, and Resources.	It is imperative that candidate vaccines, therapeutics, adjuvants, diagnostics and resources against selected infectious biological threat agents be developed as quickly as possible to reduce the threat of their use in acts of terrorism or war. The interaction of industry or non-profit organizations with academic organizations (if applicable) and the Government is strongly encouraged to quickly transition candidate products through preclinical development and clinical testing and commercialization. This partnership program will support the clinical development of specific high priority products beginning with the further characterization of the candidate through preclinical development and Phase I and/or Phase II clinical studies.	RELEASE DATE: November 14, 2002 (see NOT-AI-03-006), Program Announcement: PAR-03-025

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Partnerships for Novel Therapeutic, Diagnostic, and Vector Control Strategies in Infectious Diseases	The objective of this program is to support the development drugs and diagnostics for human infectious diseases of public health importance and products for controlling arthropod vectors that transmit infectious agents. This PAR emphasizes areas that could have a high impact on public health, but currently appear not to be a high priority or that may be considered too financially risky for industry. In addition, research on agents of bioterrorism concern are of high priority. Projects supported should have the ultimate go of producing a novel therapeutic, diagnostic tool, or vector control agent or strategy that adds substantively to the curre armamentarium for control of an infectious disease that causes a significant public health burden but is not a current priority for industry research and development.	Release Date: December 4, 2001 PA NUMBER: PAR-02-026 (also see addenda NOT-AI-02-022, NOT-AI-02-013, NOT-AI-02-007) National Institute of Allergy and Infectious Diseases Letter of Intent Receipt Date: February 20, 2002 Application Receipt Date: March 20, 2002
USDA	Development of a rapid, sensitive and specific PCR-based test for detecting multiple AR*Salmonella typhimurium* DT104 (DT104)	ARS developed this test to provide the basis for rapid pre- and/or post-harvest detection of an important foodborne pathogen. The implementation of this test will reduce the time needed to detect DT104 from 24- 48 hours to 8-12 hours. That is, potentially contaminated meat could be detected before leaving the slaughterhouse. This system was combined with a similar test for E. coli O157:H7 so that both pathogens could be detected simultaneously.	Ongoing: USDA-ARS: Ames, IA - National Animal Disease Center (NADC).
USDA	Determination of the virulence of *Enterococci* bacteria	ARS scientists developed a multi-plex PCR for Enterococci. This assay enabled scientists to rapidly identify and differentiate Enterococcal strains which have the potential to cause disease. Unlike current methods which are time consuming, inaccurate, and costly, this PCR assay is rapid, accurate and cost-effective.	Ongoing: USDA-ARS: Athens, GA.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
USDA	New methods for the determination of AR in *Campylobacter*	Antimicrobial test methodologies for *Campylobacter* are technically difficult, costly and often difficult to compare to agar dilution which is considered the 'gold standard'. A microbroth dilution assay has been developed which is cost effective, comparable to existing methodologies, easier than the agar dilution, and compatible with current equipment to determine antimicrobial susceptibility in *Campylobacter* species. This work will be presented to the National Committee for Clinical Laboratory Standards (NCCLS) for adoption as a recommended testing methodology. NCCLS determines the most accurate means of antimicrobial susceptibility testing and disseminates this information worldwide.	Ongoing: USDA-ARS: Athens, GA.
USDA	Identification of collagenase secreted by Salmonella typhimurium DT 104 and the development of a RT-PCR assay for collagenase expression	In a recent study, we identified a collagenase secreted by DT104. The collagenase identification was based on DNA sequence homology to an *E. coli c* collagenase. Also, we could reconstitute the cytotoxic phenotype by introducing the collagenase gene into a collagenase(-) strain. This collagenase is expressed and secreted only under certain conditions that seem to be determined by the host. We have developed an RT-PCR assay for collagenase expression, an we will be using this assay to identify other strains that exhibit the cytotoxic phenotype. In a different line of research, we found that the integron structure in DT104 is not stable.	Ongoing. NADC, Ames IA
USDA	Develop pre-harvest version of the USDA-FSIS FAST	The University of Nebraska will develop a more cost-effective test for detecting antibiotic-resistant bacteria. Educational materials will also be produced.	Ongoing. Griffins, University of Nebraska.
USDA	Evaluation of a micro broth dilution assay for antimicrobial susceptibility testing of Campylobacter	A microbroth dilution assay has been developed which is cos effective, comparable to existing methodologies, easier than the agar dilution, and compatible with current equipment to determine antimicrobial susceptibility in Campylobacter species. This work was funded through a CRADA with the Animal Health Institute and will be presented to the National Committee for Clinical Laboratory Standards (NCCLS) for adoption as a recommended testing methodology.	Ongoing. Russell Research Center, Athens. Georgia.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
USDA	Development of a PCR assay for detection of mixed cultures in Campylobacter	We have developed a PCR assay which identifies mixed populations of Campylobacter. This PCR assay is ideal for applications with high throughput requirements, such as ofte occurs within our unit.	Ongoing. Russell Research Center, Athens, Georgia.
USDA	Development of a rapid PCR assay for genus and species identification of enterococci	We developed a multiplex PCR procedure in conjunction with a colony PCR method that will identify the genus and the species of 25 Enterococcus strains that have been isolated and classified. Primers specific for the genus have been combined in 7 different reaction mixtures to primers for the different species and from bacterial culture to finish, the entire process requires approximately 3 ½ hours. The procedure is a cost-effective, rapid, and accurate method for identification of enterococci and an application for a patent is currently being pursued.	Ongoing. Russell Research Center, Athens, Georgia.
Action Item #77: Encourage Basic and Clinical Research in Support of the Development and Appropriate Use of Vaccines in Human and Veterinary Medicine in Partnership with Academia and the Private Sector.			
NIH, USAID	Randomized, double-blinded, controlled Phase III efficacy trial of pneumococcal conjugate vaccine	NIAID is conducting a randomized, double-blind, controlled Phase III efficacy trial in The Gambia, West Africa, using a 9-valent pneumococcal conjugate vaccine manufactured by Wyeth-Lederle Vaccines and Pediatrics (WLVP). The trial is designed to determine the impact of the pneumococcal conjugate vaccine, when administered with DPT/Hib (Tetramune™) in the same syringe, on childhood mortality due to invasive pneumococcal disease. The main endpoint will be overall mortality; however, secondary endpoints will include the effect of the vaccine on mortality and on invasive pneumococcal disease caused by pneumococci of vaccine serotype. Approximately 16,000 children will be recruited into the trial from shortly after birth over a period of 3 and a half years. Three doses of the DTP/Hib vaccine mixed with the 9-valent pneumococcal conjugate vaccine will be administered to half the children at two, three, and four months of age. Th other half will receive just the DTP/Hib vaccine.	Initiated, phase III trial. It is anticipated that the trial will last a period of 5 years.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CDC	Measuring the effectiveness of pneumococcal conjugate vaccine for children: assessing the impact on drug-resistant *Streptococcus pneumoniae* (DRSP)	A 7-valent conjugate vaccine for *Streptococcus pneumoniae*, licensed by the FDA in 2000, is recommended by the Advisory Committee on Immunization Practices for children <5 years. Three CDC projects assess the effectiveness of this vaccine in preventing pneumococcal infections, including drug-resistant infections: 1) a case-control study of vaccine effectiveness in preventing invasive infections in children in 9 Emerging Infections Program areas in which population-based active surveillance is conducted; 2) an assessment of the impact on nasal colonization of children living in Anchorage, Alaska through annual culture surveys; 3) a community wide study of colonization in remote Alaska villages before and after introduction of the vaccine to assess the impact of the vaccine on carriage of drug-resistant strains among vaccinees and nonvaccinees. Data from these studies will be used to evaluate vaccine recommendations in the U.S. Decision makers in other countries will use these data to determine whether pneumococcal conjugate vaccine should be used.	Ongoing. During 2000 and 2001 the study protocol was developed, a pilot study was launched, and procedures manuals and tracking system were revised in preparation for the main study. During 2002, cases and controls were enrolled and main data collection began. Interim analysis indicates that the vaccine is very (>90%) effective against disease caused by pneumococcal serotypes in the vaccine and serotypes closely related to those in the vaccine. (Whitney CG, et al.; Decline in invasive pneumococcal disease after the introduction of protein-polysaccharide conjugate vaccine. N. Engl. J. Med. 2003 May 1;348(18):1737-46).
DoD	Double-blind placebo-controlled clinical effectiveness trial of the 23-valent pneumococcal vaccine	*S. pneumoniae* is a leading cause of morbidity in the U.S., causing an estimated 500,000 cases of pneumonia, 3,000 cases of meningitis, 50,000 cases of bacteremia, and 7,000,000 cases of otitis media annually. Navy data from 1981 to 1991 suggest that *S. pneumoniae* causes approximately 12% of pneumonia hospitalizations in the military or 9.5 admissions per 100,000 person-years. A 23-valent pneumococcal vaccine is being used at one military basic training facility and at military training facilities. This vaccine provides coverage for 85 - 90% of the serotypes causing bacteremia in the general population, but its clinical benefit needs to be more fully characterized before the impa of its use on the emergence or spread of *S. pneumoniae* resistance can be determined.	Ongoing. Results are available to the military training facilities and are being presented at national meetings and in publications.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
FDA	Vaccine research	Research in support of the development and appropriate use of vaccines in humans to: 1) prevent viral infections, i.e. influenza, RSV; 2) prevent common bacterial infections i.e. *S. pneumoniae*, non-typable *Haemophilus influenzae*, group B streptococcus, *N. gonorrhoeae*, *N. meningitidis*.	Twelve ongoing research projects support development of vaccines for the organisms listed: 1) Completed study of protective levels of antibody against neonatal type 1a group B streptococcal infection (funded through interagency agreement with NICHD). 2) Ongoing research regarding correlates of protection against other common types of group B streptococcus. 3) Investigating correlates of protection against infection with *Streptococcus pneumonia*. 4) *N. gonorrhoeae.* Studying immunogenicity and pathogenicity of associated proteins, funded through the FD. Office of Women's Health.
FDA	Vaccine development	Research in support of the development of vaccines to prevent colonization, infection, and transmission of tuberculosis	Current projects investigate the following vaccine candidates in mouse model of tuberculosis: combination DNA vaccines, multigene DNA constructs, attenuated live vaccines and subunit vaccines. These vaccines are also being tested using prime-boost strategies and post-exposure models.
FDA	Multidrug resistant TB	Research: mechanisms of resistance in multidrug resistant tuberculosis.	Identified genetic mechanisms for multiple mechanisms of drug resistance in *M. tuberculosis.*
FDA	Drug therapy	Research: novel targets for drug therapy (to avoid resistance).	Two ongoing projects that examine the mechanisms of development of HIV drug resistance.
NIH	Phase One safety trial of a group B streptococcal type V polysaccharide-tetanus toxoid conjugate vaccine in healthy adults	NIAID is the sponsor of a Phase 1 safety trial of a group B streptococcal type V polysaccharide-tetanus toxoid conjugate vaccine in healthy adults, 65-85 years old. The vaccine was well tolerated in all volunteers.	Future plans include serological testing and data analysis.
NIH	Phase One safety trial of a group A streptococcal vaccine	NIAID is the sponsor of a Phase one safety trial of a group A streptococcal vaccine consisting of a live oral commensal bacterium, *Streptococcus gordonii* SP204(1-1) that will serve as a vector for a conserved region of the M6 protein of *Streptococcus pyogenes*. At University of Maryland's Center for Vaccine Development (a Vaccine and Treatment Evaluation Unit under contract with DMID/NIAID), a clinical trial has been completed with the vector. *S. gordonii* SP204(1-1) was implanted in healthy adults via the oral and nasal routes and found to colonize all volunteers. The vector strain was well tolerated and was successfully eradicated (spontaneously or following treatment with azithromycin).	Ongoing.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Hexavalent group A streptococcal vaccine evaluation	NIAID is the IND sponsor for a safety and immunogenicity clinical trial to evaluate a hexavalent group A streptococcal vaccine consisting of a recombinant fusion protein containing the amino-terminal M protein fragments from 6 serotypes.	Conducting a phase one clinical trial at the University of Maryland's Center for Vaccine Development, which is to be completed in 2003.
NIH	Pneumococcal group C conjugate vaccine evaluation	A double-blinded, randomized efficacy trial was conducted in Navajo and Apache Native American children who received either the conjugate pneumococcal vaccine or a control vaccine (i.e., meningococcal group C conjugate). Nasopharyngeal samples were collected from family members of children who participated in the trial. Results suggest that community-wide use of the pneumococcal conjugate vaccine reduces carriage of vaccine type strains in both adult family members and unvaccinated children who had direct or indirect contact with their siblings who were immobilized with the 7-valent pneumococcal conjugate vaccine. This reduction could be due to decreased circulation of these strains at the family or community level. Overall carriage was not decreased, suggesting that replacement with non-vaccine type strains may be occurring	These data overall suggest that widespread use of the pneumococcal conjugate vaccine among children may change the distribution of pneumococcal serotypes within communities.
NIH	Double-blind, randomized, controlled multi-center tria in older adults to an experimental 9-valent conjugate pneumococcal vaccine compared with the conventional 23-valent pneumococcal polysaccharide vaccine	Elderly individuals are at an increased risk for serious pneumococcal infection. Understanding and improving the response to pneumococcal vaccine in persons over the age of sixty-five is an important step in preventing this serious illness. To address this issue, a double-blind, randomized, controlled multi-center trial was conducted to evaluate the relative safety and immune response to an experimental 9-valent conjugate pneumococcal vaccine compared with the conventional 23-valent pneumococcal polysaccharide vaccine in older adults. The response to revaccination following conjugate vaccine is also being evaluated. Outcome measures include adverse effects, serotype specific antibody responses as well as antibody responses to carrier protein, effects on functional antibody status and on nasal carriage of *S. pneumoniae.*	The conjugate vaccine has been administered to 180 elderly volunteers and has been shown to be extremely safe. Immunogenicity data awaits analysis.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Expanded Phase II and IV Vaccine Trials in Humans Contracts	In November 2001, NIAID awarded four contracts based on proposals received from the solicitation "Expanded Phase II and IV Vaccine Trials in Humans." The objective of these contracts is to provide clinical investigators, facilities and subjects for the conduct of clinical trials requiring rapid and efficient enrollment. The types of clinical trials implemented under this contract will be Phase II and IV vaccine immunogenicity and safety studies of investigational and licensed vaccines.	Archived electronic request for proposal: [URL] www;niaid.nih.gov/contract/archive/RFP0203.pdf
NIH	Scientific Advance: Group B streptococcal C5a peptidase is both a specific protease and mediates fibronectin binding.	Group B streptococci (GBS) are a major cause of pneumonia, sepsis and meningitis in neonates and a serious cause of mortality and morbidity in immunocompromised adults. C5a peptidase is a GBS surface protein which was shown previously to be involved in the pathogenesis of GBS infections because of the protease activity of the molecule. This activity involves the cleaving and inactivation of C5a, a component of the human complement system and thus contributes to the ability of GBS to evade phagocytosis. Two recently published papers provide data suggesting that C5a peptidase also contributes to the pathogenesis of GBS infections by mediating fibronectin binding. The importance of the recent finding is that binding of fibronectin has been implicated in attachment and invasion of eukaryotic cells by streptococci. These data therefore demonstrate that this protein may provide a mechanism for GBS colonization of epithelium and subsequent infection, and may serve as a potential vaccine target for Streptococci.	Cheng Q, Stafslien D, Purushothaman SS, and Cleary P: The Group B streptococcal C5a peptidase is both a specific protease and an invasion. Infect Immun 70:2408-2413, 2002. Beckmann C, Waggoner JD, Harris TO, Tamura GS and Rubens, CE: Identification of novel adhesions from Group B streptococci by use of phage display reveals that C5a peptidase mediates fibronectin binding. Infect Immun 70:2869-76, 2002 Award data: R01AI20016, Patrick Cleary, University of Minnesota R01AI30068, N01AI75326, Craig Rubens, University of Washington

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Scientific Advance: Lethal synergism described between influenza and pneumococcus.	Many bacteria and viruses carry an enzyme called a neuraminidase, which functions to cleave the molecule sialic acid from the surface of cells. Data indicate that viral neuraminidase plays a crucial role in priming the lung for adherence and infection by bacteria such as the pneumococcus. Receptors for the pneumococcus, normally hidden by sialic acids, are uncovered by pre-infection with influenza and become available throughout the lung for bacterial infection resulting in a widespread and severe pneumonia. Blocking the activity of the viral neuraminidase with a new class of anti-influenza drugs, the neuraminidase inhibitors, prevents synergistic pneumonia and death. This discovery has important implications; use of these drugs in humans either during, or even, after cases of influenza might protect against development of pneumonia and serve to minimize the emergence of AR. As this is a leading cause of death particularly in the elderly, this finding could have a major impact on health in the United States and the world.	Cullers JA, Rehg JE: Lethal synergism between influenza virus and *Streptococcus pneumoniae*: characterization of a mouse model and the role of platelet activating factor receptor. J Infect Dis, 186:341-350, 2002. Award Data: K08 AI 49178; Jonathan A. McCullers; St. Jude Children's Research Hospital
NIH	Scientific Advance: Variable Gene Defects Described Relating to Pneumococcal Susceptibility	Studies in the past year revealed that human antibodies to serotype three pneumococcal capsular polysaccharide are derived from VH3 gene elements. Antibodies to other serotypes also use VH3 genes. This is an important finding, because VH3 dysregulation is found among patients who are at unusually high risk for the development of pneumococcal disease, including individuals with HIV infection and those who have undergone bone marrow transplantation. Based on the fact that increased rates of pneumococcal disease occur in patient groups that manifest VH3 dysregulation, researchers hypothesized that a 'hole' in the antibody repertoire translates into increased susceptibility to pneumococcal disease and an inability to respond to existing vaccines. Plans are now in progress to investigate these mechanisms and to develop alternative therapies, vaccines, and diagnostic tools to assess whether or not an individual has generated antibodies to serotype 3 that are likely to be protective.	Pirofski L: Polysaccharides, mimotopes, and vaccines for encapsulated pathogens. Trends Microbiol 9: 445-452, 2001. Award Data: R01 AI 44373; Lise-Anne A. Pirofski; Albert Einstein College of Medicine

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Scientific Advance: Scientists Describe Role of Opacity Variation in Pneumococcal Susceptibility	Colonization of the nasopharynx is the initial step in all infections caused by Streptococcus pneumoniae. The antibody response to carriage was examined in an experimental model of human colonization in healthy adults. Asymptomatic colonization was detected in 6/14 subjects an continued for up to 122 days. Susceptibility to carriage did n correlate with total serum immunoglobulin (IgG) to the phenotypic capsular polysaccharide. All of the colonized subjects, in contrast, developed a serum IgG and secretory IgA response to a 22 kD protein, whereas 7 of 8 subjects wh did not become colonized had preexisting antibody to this protein. Analysis of the 22 kD protein identified it as the NH(2)-terminal region of pneumococcal surface protein A (PspA). These findings provide evidence for the role of antibody to this protein fragment in preventing pneumococcal carriage by humans. These studies point the way to the potential for a protein-based vaccine that could block the critical first step in pathogenesis, and ultimately decrease infections and the need for antimicrobial therapy.	McCool TL, Cate TR, Moy G, and Weiser JN: The immune response to pneumococcal proteins during experimental human carriage. J Exp Med. 195: 359-365, 2002. Award Data: R01 AI 38446; Jeffrey N. Weiser; University of Pennsylvania
NIH	Scientific Advance: Development of a Vaccine for Nontypeable *Haemophilus influenzae*	The outer membrane protein, P6, is undergoing testing as a vaccine for nontypeable *H. influenzae*. One of the key questions to answer when developing vaccines is whether an immune response to a vaccine will actually protect from infection by the bacterium, called the protective immune response. To determine whether an immune response to P6 is protective, a series of assays on the lymphocytes (white blood cells) of adults with COPD was performed. Ten patients who had exacerbations caused by nontypeable *H. influenzae* in the previous twelve months had a significantly lower response to P6, compared to twenty-six patients with n exacerbations in the previous twelve months and twelve healthy age-matched controls. These results indicate that an immune response to P6 is associated with protection from infection by nontypeable *H. influenzae*. In addition, this is the first time an immune response to a specific antigen has been shown to be associated with protection from exacerbations of COPD. These results provide further rationale to proceed with human trials to test the efficacy of P6 as a vaccine antig	Abe Y, Murphy TF, Sethi S, Faden HS, Harabuchi Y, Thanavala YM: Lymphocyte proliferative response to P6 of nontypable *Haemophilus influenzae* is associated with relative protection from exacerbations of chronic bronchitis. American Review of Respiratory and Critical Care Medicine 165: 967-971, 2002. Award data: R01 AI19641-18, Timothy F Murphy, State University of New York at Buffalo

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Vaccine Action Program	The INDO-US Vaccine Action Program initiated in 1987 is a bilateral program that focuses on the development of safe ar effective vaccines for major communicable diseases of interest to the two countries through joint research and development efforts.	Currently, the focus of the program is on HIV/AIDS, malaria, and tuberculosis.
NIH	Adult efficacy trial using acellular pertussis vaccine	An adult efficacy trial using acellular pertussis vaccine was recently completed in 2,784 subjects 15-65 years of age to define the incidence, clinical spectrum, and epidemiology of pertussis infection and disease in adolescents and adults as well as define the safety, immunogenicity, and efficacy of an acellular pertussis vaccine designed for use in older individuals. The acellular vaccine was shown to be safe with no vaccine associated serious adverse events. Confirmed pertussis occurred in two vaccines and 9 controls, yielding a efficacy of 77%. This estimate of efficacy is similar to that observed in young children.	These data suggests that an acellular pertussis vaccine give to adolescents and adults in the form of a dTaP booster would be safe and effective in reducing the burden of diseas in this population in addition to reducing secondary transmission to infants.
NIH	Prospective, randomized, double-blinded, controlled, multisite trial of acellular pertussis vaccine in healthy adults and adolescents	Pertussis is a preventable cause of cough illness in all age groups, but is rarely considered or diagnosed in older childre or adults. Both natural and vaccine-induced immunity to pertussis wanes, resulting in repeat infections throughout life and an opportunity for transmission to susceptible infants. An adult efficacy trial using acellular pertussis vaccine was recently completed in 2,784 subjects 15-65 years of age to define the incidence, clinical spectrum, and epidemiology of pertussis infection and disease in adolescents and adults as well as define the safety, immunogenicity, and efficacy of an acellular pertussis vaccine designed for use in older individuals.	The acellular vaccine was shown to be safe with no vaccine associated serious adverse events. Confirmed pertussis occurred in two vaccinees and 9 controls, yielding an efficacy of 77%. This estimate of efficacy is similar to that observed in young children. Extensive experience in children suggests that an acellular pertussis vaccine given to adolescents and adults in the form of a dTaP booster would be a safe and effective means for reducing the burden of disease in this population, in addition to reducing secondary transmission to infants.
NIH	Respiratory syncytial virus (RSV) vaccine trial in healthy third-trimester pregnant women	NIAID is the sponsor of a randomized, double-blinded, placebo controlled, Phase one safety trial at Baylor College, utilizing an RSV subunit vaccine in healthy third-trimester pregnant women. All enrolled subjects were vaccinated and delivered healthy babies (last clinical observations were in May 2001).	Sample collection and analysis is ongoing.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Hyperaccelerated Award/Mechanisms in Immunomodulation Trials	In 2002, this research initiative was expanded to include support for research grants to study immunological mechanisms in clinical trials of vaccines. The aim is to facilitate studies of human immunologic function in vaccination, including analyses of the underlying mechanism of protective immunity, specificity and kinetics of immune responses, and immune memory. Proposed studies must make use of clinical samples from a parent clinical trial that is supported by other funding.	FA (AI-02-003). Awards to be made in 2003.
NIH	Immune Epitope Database and Analysis Program	The primary purpose of this research program is to design, develop, populate, and maintain a publicly accessible, comprehensive Immune Epitope Database containing linear and conformational antibody epitopes and T cell epitopes composed of MHC-binding peptides and ligands (e.g., carbohydrates, lipids, and modified peptides) with priority for epitopes associated with CDC category A-C potential bioterrorism pathogens and their toxins. The Immune Epitope Database will be freely accessible to the scientific community via an Internet website and will include an Analysis Resource containing analytical software tools that will be developed and maintained by the contractor.	RFP (DAIT-03-31). Award is expected in late 2003.
NIH	Innate Immune Receptors and Adjuvant Discover	The purpose of this research project is to solicit proposals for a research program beginning at the discovery/molecular response evaluation stage and progressing to preclinical testing of new adjuvants based upon triggering of the human innate immune system. The adjuvant products aimed for in this program may encompass uses both as vaccine adjuvants, to elicit T- and B cell responses when co-administered with an immunogen, as well as stand-alone immunomodulators to stimulate short term protective responses against broad categories of infectious agents. Research must be directed toward vaccine adjuvants and immune stimulation strategies to defend against CDC categories A, B, or C agents.	RFP (DAIT-BAA-03-41). Multiple awards will be made in late 2003.
NIH	Millennium Vaccine Initiative-Novel Vaccines for Tuberculosis and Malaria	The goal of this contract solicitation is to increase collaboration between industry and the public sector to promote the development of new vaccines to prevent tuberculosis and malaria in developing countries using existing technology platforms.	RFP (AI 02-15). Award made to Epimmune, for development of a novel malaria vaccine in collaboration with NIAID and the Naval Medical Research Center.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
Action Item #78: Encourage Basic and Clinical Research in Support of Novel Approaches to Preventing or Treating Infections with Resistant Organisms That Occur in Humans and Animals by Partnering with Academia and the Private Sector.			
NIH, NSF, USDA	International Cooperative Biodiversity Groups Progra (ICBG)	International Cooperative Biodiversity Groups Program (ICBG) has a 3 fold mission: conservation of biodiversity, economic growth for developing countries, and discovery of pharmaceuticals from natural products. The ICBG program is a model for research partnerships by acknowledging intellectual property ownership of indigenous communities.	Currently 6 awards have been made to multidisciplinary research groups that also include in-country, research-capacity strengthening activities, community education programs, ethnobotanically-based plant collections, and partnerships with a pharmaceutical company. ICBG investigators have achieved extensive progress identifying bioactive compounds from plants of Central and South America, Nigeria, Cameroon, Madagascar, Laos, and Viet Nam.
CDC, NIH, USAID	Global Alliance for TB Drug Development	The Global Alliance for TB Drug Development is a new public/private partnership to stimulate new drug development against tuberculosis. NIAID is involved in this collaboration with private partners, who are contributing to the development of new drugs to shorten the treatment of TB and facilitate its control in the poorest countries. Over 30 organizations are stakeholders in this innovative public-private partnership, including the Bill & Melinda Gates Foundation, CDC, NIAID/NIH, Rockefeller Foundation, USAID, the World Bank, and WHO. For a comprehensive list, see; http://www.tballiance.org	NIAID staff assisted the Global Alliance for TB Drug Development in developing a process for soliciting requests for drug discovery and development proposals from the glob research and development community and in the scientific peer review of the proposals. Of the 107 proposals received, eleven were identified for potential support by the Global Alliance for TB Drug Development as preclinical candidate compounds or as clinical trials of new drug regimens. Of these, a nitroimidazole antibiotic compound (PA-824) has been identified as a potential candidate for development into new anti-TB drug by the TB Alliance. Issues such as synthesis, toxicology testing, and formulation are being examined for feasibility. [Nature 2000 405:962-966]
FDA	Guidance document	Guidance document: Biologics Derived from Bioengineered Plants for Use in Humans and Animals	Working group formed; Draft document completed.
NIH	Challenge Grants	Through a special appropriation from Congress, a new government/industry partnership was set up with industry matching NIAID funds 1:1, using milestone-driven goals for evaluation and allowing substantive involvement on the part of NIH. NIAID funds are being matched with industry funds from Sequella Inc. to develop improved drugs for TB treatment, Glaxo SmithKline to develop drug candidates against TB and other bacterial infections, and Corixa Corp. to conduct preclinical testing of new TB candidate vaccines.	Ongoing.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Pharmaco-economics report on TB drug development	Through participation in the Global Alliance for TB Drug Development, many NIAID-supported investigators and staff contributed to a publication detailing the investments and potential markets required to develop a new drug for the treatment of TB. The NIAID TB Technology Transfer contractor (Research Triangle Institute of North Carolina) organized, researched, coordinated, and edited a major repo on the economic factors involved in bringing a new anti-tuberculosis drug to market. This report will be a rigorous, authoritative source of information on the epidemiology of TB, potential market for new anti-TB drugs, cost of TB drug development, and options for funding and conducting drug development. The report will provide data required for informed investment decisions by industry, foundations, government organizations, and world health and financial organizations.	Available on the Global Alliance for TB Drug Development website, http://www.tballiance.org.
NIH	Workshop on Longer Acting Rifamycins	Meeting organized by the Global Alliance for Tuberculosis Drug Development and was focused on the "Role of Longer Acting Rifamycins for Treatment of Tuberculosis". Bringing together investigators involved in all phases of TB drug development, the workshop sought to recommend a strategic approach for the TB Alliance regarding the evaluation of long acting rifamyins such as rifapentine and rifalazil for TB treatment and prevention. In attendance were representatives from the pharmaceutical industry, NIAID (DAIDS, DMID and DIR), CDC, FDA, infectious disease physicians, and NIAID-supported investigators including participants of the TBRU. The primary recommendations were to explore the clinical potential of the newly licensed rifapentine and to screen for more potent and less toxic rifamycins from among libraries of candidate compounds.	Held in Bethesda, MD on April 8-9, 2002
NIH	Tuberculosis Antimicrobial Acquisition and Coordinating Facility (TAACF)	New drugs to treat TB are being screened through this NIAID contract. Southern Research Institute in Birmingham, Alabama has established a facility to acquire compounds for screening against Mtb, maintain a computerized chemical database of compound structures, coordinate and distribute compounds for evaluation *in vitro* and in an animal model, and report data back to suppliers.	The TAACF has contacted over 3,500 chemists throughout the world seeking candidate anti-TB compounds. Over 60,000 compounds have been received from academic and private sector investigators, principally in the United States and Europe, with growing involvement of scientists from Africa, Asia, Australia, South America, and other geographic sites; http://www.taacf.org

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Submission of compounds for *in vitro* evaluation	Staff have selected for evaluation more than 10,000 compounds, based on their chemical structure, from the National Cancer Institute (NCI) chemical repository of over 500,000 compounds. Of these compounds, 500 have shown initial *in vitro* activity against a wild-type strain, and of these, approximately 100 have promising *in vitro* activity against isoniazid (INH)-resistant strains. A large part of this effort is conducted under an interagency agreement with the Health Resources and Services Administration at the Gillis W. Long Hansen's Disease Center. Efficacy evaluations in animal models of TB are being conducted on selected compounds.	Ongoing.
NIH	High-throughput screening contract (N01-AI-15449) with Southern Research Institute	This contract awarded to Birmingham, Alabama in response to RFP AI01-13, "Tuberculosis Drug Screening: Part B" will provide a high throughput screening capability to develop and implement biochemical, target-specific Mtb drug screening assays and to develop and implement Mtb metabolic stage-specific drug screening assays.	Ongoing.
NIH	Therapeutics Research on AIDS-Associated Opportunistic Infections and Malignancies	Goal is to stimulate iterative preclinical research for novel therapeutic strategies against opportunistic infections, co-infections, and malignancies in people with HIV/AIDS. The PA is a joint sponsorship with the National Cancer Institute and the National Institute of Dental and Craniofacial Research. The AIDS-associated infections emphasized by this PA are tuberculosis, *Pneumocystis carinii* pneumonia, *Cryptosporidium parvum*, and the microsporidia. The AIDS-associated malignancies emphasized by this PA are Kaposi's sarcoma, lymphomas, cervical cancer, oral warts and cancers, and anogenital cancers.	PA-01-113 grants awarded in 2002: R. Reynolds (Southern Research Institute) Inhibition of FtsZ Polymerization in M. tuberculosis J. Welch (SUNY Research foundation) A New Target for Ant TB Agents, Fas I. R. Barletta (University of Nebraska) Targeting M. tuberculosis Alanine Ligase for Drug Design W. Atkins (University of Washington) Glutamine Synthetase Inhibitors for Tuberculosis Therapy C. Nacy (Sequella Global TB Foundation) Gene-based and whole Bacteria High -throughput TB screens.
NIH	Four National cooperative drug discovery groups (NCDDG-OI) are working on TB drug discovery	In order to stimulate private sector involvement in the development of drugs for TB, three NCDDTG (P. Brennan, Colorado State University; L. Heifets, National Jewish Center; W. Jacobs, Albert Einstein University; J. Sacchettini, Texas A&M University) actively collaborated with pharmaceutical firms with an interest in TB drug development (Glaxo SmithKline). A fourth NCDDG is studying the Mtb alanine racemase for targeted drug design (Kurt Krause, University o Houston).	Collaborations ongoing.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Scientific Advance: *Haemophilus*: Ramifications of pilus-mediated adherence	A recent finding demonstrated that an important component of the host response to non-typeable *Haemophilus influenzae* (NTHi) infection, i.e., the elaboration of nitric oxide (NO) and nitric oxide-related molecules, may be a prime mediator in the disruption of tight junctions (TJ), protein arrays that function to seal epithelial cells together. By analyzing multiple components that comprise the TJ, NIAID-supported scientists found that two proteins in particular (ZO-1 and ZO-2) were displaced from this structure during either NTHi infection or when exposed to NO alone. Coincident with this disorganization of TJ proteins is an increase in the leakiness of the epithelium and a greater rate of bacterial invasion. By inhibiting the release of NO, these investigators were able to prevent NTHi-mediated TJ changes and thereby close one route to which this organism takes to invade the human airway. This work may provide a rationale for future therapies based on modulating the human inflammatory response in combination with antimicrobial agents.	Krasan GP, and Madera RT: Induction of nitric oxide and nitrosative stress during *Haemophilus influenzae* infection. In Press. Molec. Microbiol., 2002. Award data: K08 AI 01801; Graham P. Krasan; University of Michigan
NIH	Scientific Advance: Moxifloxacin is a promising new antibiotic for tuberculosis	Moxifloxacin is a new quinolone antibiotic shown to have potent bactericidal activity against TB in an animal model of acute infection. Daily dosing of the antibiotic in levels equivalent to those used in humans reduced the levels of TB in the spleens and lungs of infected mice. The effect was comparable to isoniazid (INH) – one of the most potent drugs ever discovered to treat tuberculosis. The maximum bactericidal effect was seen with daily doses of 400 mg/kg, whereas weekly dosing was not as effective. Because of the favorable pharmacokinetic properties of moxifloxacin, this advance suggests that in combination with other longer actin antibiotics, the potential exists to shorten the course of antituberculous therapy or to allow more intermittent (i.e., once-weekly) therapy. Further studies are planned to explore this possibility in the mouse model of TB and in controlled human clinical trials. This product may provide additional options for treating MDR TB that would increase therapy compliance.	Yoshimatsu, T, Nuermberger, E, Tyagi, S, Chaisson, R, Bishai, W, and Grosset, J: Bactericidal activity of increasing daily and weekly doses of moxifloxacin in murine tuberculosis. Antimicrob Agents Chemother 46: 1875-1879, 2002. Award Data: R01 AI43846; W. Bishai, Johns Hopkins University

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Scientific Advance: Mycobacterium tuberculosis Immune Evasion Tactics Described	TB is an intracellular pathogen that survives inside the compartments of immune cells called macrophages. One of the functions of macrophages is to trigger T cell-mediated immune responses against pathogens by processing and presenting pathogen molecules, termed antigens, to CD4 an CD8 T cells. CD4 T cells play a critical role in controlling TB infections in humans, but do not completely eradicate infection. A small number of TB organisms survive inside host macrophages and evade the immune system. In this article, Dr. Harding and colleagues use biochemical analyses to define immune evasion mechanisms that occur early in infection and may enhance TB survival in the host. They found that live TB infection disrupts macrophage antigen processing events that occur soon after infection, resulting in decreased CD4 T cell responses against TB. Enhancing macrophage activation, through addition of the specific growth factor interferon-gamma, improves CD4 T cell responses. These studies will aid the development of novel immunotherapeutics against the pathogen.	Ramachandra L, Noss E, Boom WH, and Harding CV: Processing of Mycobacterium tuberculosis antigen 85B involves intraphagosomal formation of peptide-major histocompatibility complex II complexes and is inhibited by live bacilli that decrease phagosome maturation. Journal of Experimental Medicine 194:1421-1432, 2001. Award Date: R01 AI 34343 and 35726; Clifford V. Harding, Case Western Reserve University
Focus Area IV: Product Development			
**** TOP PRIORITY **** **Action Item #79: Create An Interagency AR Product Development Working Group To Identify and Publicize Priority Health Needs in Human and Animal Medicine for New AR Products (e.g., Innovative Drugs, Targeted Spectrum Antibiotics, Point-of-Care Diagnostics, Vaccines and Other Biologics, Anti-Infective Medical Devices, and Disinfectants).**			
FDA	Interagency AR product development working group	FDA has chosen to perform these cooperative activities using existing advisory committees with other agency and industry participation.	Initial AC meeting Feb 19-20, 2002. Docket available for additional comment.
FDA	Otitis Media Advisory Committee	Discussion of clinical study design for drugs treating acute otitis media (which may impact resistance in the pediatric population)	Meeting held on July 11, 2002.
FDA	FDA/PhRMA Co-Sponsored Workshop	Discussion of statistical issues in clinical trials including trials related to resistant pathogens.	Meeting held on November 9, 2002.
FDA	FDA/IDSA/PhRMA Co-Sponsored Public Workshop	Coordinated and hosted a public workshop that brought together top national leaders and scientists from the Infectious Disease Society of America, Pharmaceutical	Meeting held on November 19-20, 2002.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
FDA	Anti-Infective Drugs Advisory Committee (ADAC)	Discussion of issues relating to macrolide-resistant *Streptococcus pneumoniae* (MRSP)	Meeting held on January 24, 2003.
FDA	Anti-Infective Drugs Advisory Committee (ADAC)	Discussion of issues relating to AR in *Streptococcus pneumoniae*.	Meeting held on March 4, 2003.
FDA	Anti-Infective Drugs Advisory Committee (ADAC)	Discussion of a list of Antimicrobial Resistant Pathogens of Public Health Importance to assist stakeholders in the development of antimicrobial drugs related to resistant	Meeting held on May 5, 2003.
**** TOP PRIORITY **** **Action Item #80: Identify Ways (e.g., Financial and/or Other Incentives or Investments) To Promote the Development and/or Appropriate Use of Priority AR Products, such as Novel Compounds and Approaches, for Human And Veterinary Medicine for Which Market Incentives Are Inadequate.**			
FDA	New AR products	Identify and publicize priority public health needs for new AR products; identify the kinds of products we would want to see developed.	Preliminary meeting has occurred; working group is forming; future action TBD CDER advisory committee held February 2, 2002.
FDA	Joint efficacy workshop and advisory committee meeting	Identify ways to promote the development and licensure of additional pneumococcal conjugate vaccines. Joint NIAID/CBER Workshop and Vaccines and Related Products Advisory Committee addressed issues regarding measures o efficacy.	Completed February and March 2001. Workshop regarding correlates of protection for use in licensure of additional pneumococcal vaccines held Spring 2002.
FDA	See Action Item #79 (Interagency AR Product Development Working Group)	See Action Item #79 (Interagency AR Product Development Working Group).	See Action Item #79 (Interagency AR Product Development Working Group).
FDA	Maternal immunization	Development of approaches for licensure of vaccines to prevent group B streptococcal infections. CDC, NIH, FDA meeting May 1998 regarding Maternal Immunization and NIAID, NIH Advisory meeting regarding serological assays.	Continued regulatory and research effort to remove barriers to product development under current funding.
FDA	Guidance document	Guidance document: Biologics Derived from Bioengineered Plants for Use in Humans and Animals.	Working group formed; Draft document completed.
Action Item #81: Consider, in Consultation with Academia and Industry, Whether Government Has a Constructive Role To Play in Discovery of Drugs and Other Products Targeted To Address Areas Where Market Incentives are Limited and Unmet Needs Exist (e.g., Novel Antimicrobial Drugs Targeted To Specific Resistant Organisms).			
FDA, CDC, NIH	See Action Item #30 (FDA/IDSA/PhRMA Co-Sponsored Public Workshop)	See Action Item #30 (FDA/IDSA/PhRMA Co-Sponsored Public Workshop)	See Action Item #30 (FDA/IDSA/PhRMA Co-Sponsored Public Workshop)

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
FDA	New AR products	Development of Hyper-Immune Globulins	CBER role is to develop immunization protocols, assays and standards for such products.
Action Item #82: Continue Ongoing Approaches that Streamline the Regulatory Process, Including Clinical Trials and Enhanced Pre-Clinical Studies (e.g., Use of Pharmacokinetics and Pharmacodynamics Data) To Help Bring AR Products (Including Drugs, Vaccines, Diagnostics and Devices) To Market as Efficiently and As Rapidly as Possible, While Still Assuring Their Safety and Efficacy.			
FDA, CDC, NIH	See Action Item #30 (FDA/IDSA/PhRMA Co-Sponsored Public Workshop)	See Action Item #30 (FDA/IDSA/PhRMA Co-Sponsored Public Workshop)	See Action Item #30 (FDA/IDSA/PhRMA Co-Sponsored Public Workshop)
FDA	Workshop and committee meeting on efficacy	Identify ways to promote the development and licensure of additional pneumococcal conjugate vaccines. Joint NIAID/CBER Workshop and Vaccines and Related Products Advisory Committee addressed issues regarding measures o efficacy.	Completed February and March 2001 Workshop regarding correlates of protection for use in licensure of additional pneumococcal vaccines was held in Spring 2002.
FDA	Meningitis Vaccine Project (MVP)	MVP is a combined WHO Program for Appropriate Technology in Health (PATH) project to develop affordable meningococcal conjugate vaccines for Africa.	Scientific panel met in March 2003. Consortium of public, private, and non-profit organizations, and a philathropic organization (the Gates Foundation) will develop a vaccine that is critically needed in Africa.
FDA	Regulatory requirements – industry and scientific community	Clarify FDA regulatory requirements to both industry and the scientific community.	1) Down classification for devices intended to determine resistance and susceptibility to bacterial pathogens in a shortened incubation time period is completed and should simplify industry's administrative submittal process. Can be referenced to Action Item #76. 2) The special control guidance document for antimicrobial susceptibility test systems will be published soon. This will provide industry with the necessary elements for data gathering and presentation for a more efficient and timely review of these products. Can be referenced to Action Item #76 3) Presentation on regulatory requirements for tests of use in AR initiatives to the Professional IVD Roundtable (a group representing all major professional laboratory groups) on June 6, 2001. Discussion on obstacles and issues which might exist in technology transfer.
FDA	Topical micobicides	CBER/CDER working group on Topical Microbicides.	Working group formed; Draft document completed.
FDA	See Action Item #80 (Maternal Immunization).	See Action Item #80 (Maternal Immunization).	See Action Item #80 (Maternal Immunization).
FDA	See Action Item #80 (Guidance Document).	See Action Item #80 (Guidance Document).	See Action Item #80 (Guidance Document).

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
FDA	HIV Drug Resistance Genotype Assay Guidance (See Action Item #10)	Revised guidance on HIV Drug Resistance Genotype Assays. Significantly reduces the extent of studies required for clearance.	Publication pending
FDA	See Action Item #30 (Resistant Pathogens List Advisory Committee Meeting)	See Action Item #30 (Resistant Pathogens List Advisory Committee Meeting)	See Action Item #30 (Resistant Pathogens List Advisory Committee Meeting)
Action Item #83: In Consultation with Stakeholders and Expert Consultants, Identify Ways To Promote The Development of New and Alternative Veterinary Treatments and The Improved Use of Existing Therapies That Are Unlikely to Stimulate Resistance to Drugs in Human Medicine.			
Action Item #84: Streamline the Regulatory and Approval Process for Veterinary Antimicrobial Drugs and Related Products That Are Unlikely, Now or in the Future, To Result In Transfer of Antimicrobial Resistance To Humans.			